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CONTENTS

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PULMONARY AGENESIS AND HYPOPLASIA

BY

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In recent years the more frequent use of x-rays has revealed various congenital abnormalities of the lungs which had formerly passed undetected during life, since the clinical signs and symptoms may be minimal. An attempt is made here to elucidate the different pictures which may be seen in varying degrees of underdevelopment of the lungs.

For clarity of description the following nomenclature is based on Schneider's (1912) classification:

AGENESIS of a lung, where there is complete absence of lung and bronchus.

APLASIA of a lung, where there is a rudimentary bronchus and no pulmonary alveolar tissue.

HYPOPLASIA of a lung or part of a lung, where the alveolar tissue is underdeveloped.

The number of cases so far reported in the literature is about fifty. Hurwitz and Stephens (1937) review thirty-four cases and Deweese and Howard (1944) make the list up to forty-four. The majority of these recorded cases are of the first type, viz. agenesis, or complete absence of a lung, more commonly the left lung. The pleura may be partially or completely absent; the former is more common, the pleura then containing the displaced heart and mediastinal structures with some excess fluid. The pulmonary blood-vessels of the affected side are usually absent. The remaining case-reports describe severe degrees of aplasia or hypoplasia with practically no functional lung tissue; it is therefore of interest to report cases 4 and 5 where there is only partial underdevelopment of one lung associated with an anatomical abnormality of the bronchial tree, all of which complex appears to be a permanent abnormality. In contrast, cases 6 to 11 show a similar underdevelopment of one lung at birth, but the condition slowly readjusts itself to normal in two to three years.

The majority of recorded cases of maldevelopment have been in young infants diagnosed shortly before death or at autopsy, but the condition is compatible with a full span of life, as in a female who lived to seventy-two years. The sex incidence has been about equal. The common association of other congenital abnormalities in the chest or elsewhere is noteworthy. Symptoms varied from case to case and included cyanotic attacks, stridor, dyspnoea or no pulmonary complaints at all. Autopsy material commonly showed pneumonia in the opposite lung. Some cases showed maldevelopment of the whole chest wall, whilst others remained symmetrical on the two sides.

Embryology. According to Kiebel and Mall (1912) the lung bud appears early in foetal life (2·5 mm. embryo) as a rounded prominence below the laryngo-tracheal groove. Soon this divides into two pulmonary sacs (5 mm. embryo) so that in agenesis (complete absence) of one lung the disturbance must arise before this stage is reached. The pulmonary vessels develop after this (7 mm. embryo), at the same time as the pulmonary sacs are differentiating into three buds on the right and two on the left; any vascular anomaly is therefore unlikely to cause complete absence of a lung. The lung buds grow into loose mesodermal tissue, repeatedly branching to form the bronchial tree, but formation of alveoli does not begin until the sixth month of foetal life and is not complete until the last few weeks of pregnancy.

Aetiology. Killingsworth and Hibbs (1939) reviewed the literature on this subject, mentioning pressure effects from amnion or thymus or some primary vascular disturbance as a cause for the maldevelopment, but conclude that Schwalbe's (1912) explanation of a developmental error of endogenous origin affecting the pulmonary, vascular and respiratory systems, is the most likely. The latter theory gains support from the case reported by Finkelstein (1924) of a pair of uniovular female twins who lived for one week. At autopsy, one had a rudimentary left lung and the other a rudimentary right lung.

The hypertrophy of the opposite lung is probably compensatory.

Case Reports

The following series of fourteen cases fall into three groups.

I. Cases 1 to 5. Absence or permanent underdevelopment of one lung, i.e. agenesis, aplasia, or permanent hypoplasia.

II. Cases 6 to 11. Infants in the first year of life, showing displacement of heart and mediastinum with slow readjustment to normal within two or three years, probably a temporary hypoplasia.

III. Cases 12, 13 and 14. Children with a localized opacity in the x-ray. It is suggested that this may be caused by hypoplasia or atelectasis of part of a lung with no bronchial communication.

Group I

ABSENCE OR PERMANENT UNDERDEVELOPMENT OF ONE LUNG, i.e. AGNESIS, APLASIA OR PERMANENT HYPOPLASIA

Case 1. APLASIA OF THE LEFT LUNG. Sylvia S., aged one year, weight 17 lb. 12½ oz., had spent the first five months of her life in a hospital because she had vomited periodically from birth; she had had no cough. An x-ray revealed ' congenital small or absent left lung.' She was the first child, normal delivery, doubtfully full term with a birth weight of 5 lb. Talipes equino-varus was noticed at birth. The parents were healthy, but the mother had a bad fall when two months pregnant. A second child born two years later was normal.

CLINICAL EXAMINATION showed a microcephalic child not yet able to sit up; the circumference of head was 16·5 in., and the fontanelle was closed. There was congenital ptosis of both eyelids. The talipes was improving, according to the mother. The trachea felt central and the shape of the chest would have passed as normal, but was resonant to percussion both sides in front and dull on the left side behind where faint tubular breathing and distance heart sounds were heard; no apex beat was felt.

X-RAY OF THE CHEST (fig. 1) revealed a spina bifida

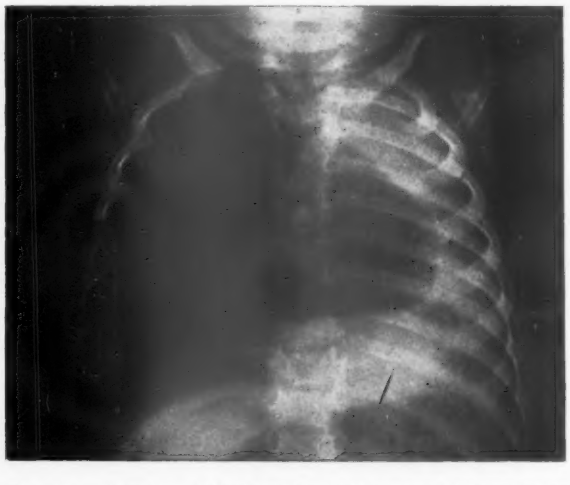

FIG. 1.—Case 1. Aplasia of the left lung with herniation of the right lung into the left chest.

in the first and second thoracic vertebrae, slight deviation of the trachea to the left and displacement of the heart to the left and backward. There appeared to be no left lung, but the right lung herniated through the anterior mediastinum to the left side.

BRONCHOSCOPY. The trachea was very narrow, and there was no sign of any main bronchus passing

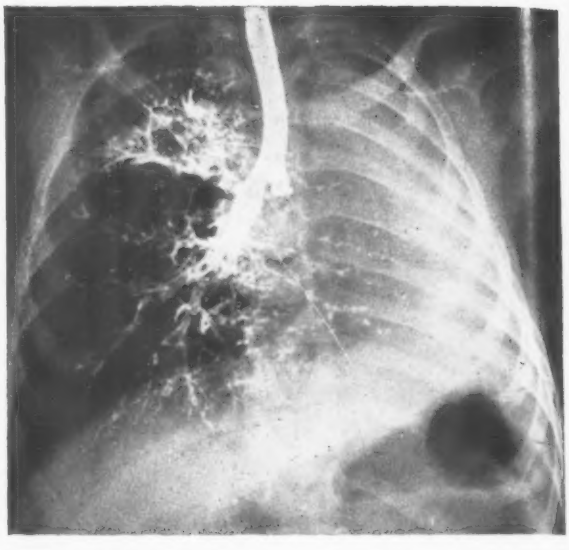

FIG. 2.—Case 1. Bronchogram, A-P view. Left main bronchus present as a stump. Right bronchial tree large, extending into the left chest.

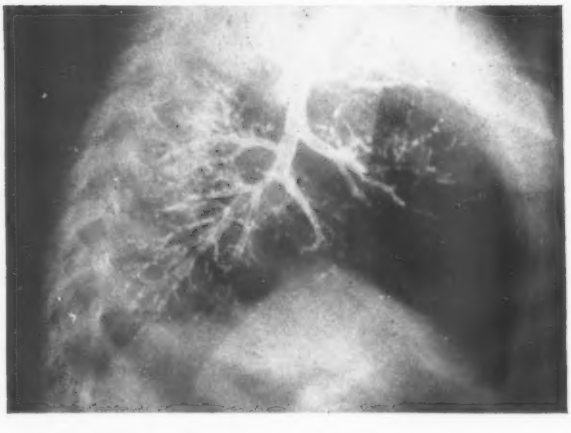

FIG. 3.—Case 1. Right lateral bronchogram. Anomalous right bronchial tree. (See case report.)

to the left lower lobe. The right main bronchus was very narrow and its main branches could not be seen. (This and subsequent bronchoscopies were kindly performed by Mr. J. Crooks.)

BRONCHOGRAM (fig. 2 and 3). The left main bronchus was present as a stump and the anomalous right bronchial tree was interpreted as showing a large pectoral branch of the upper lobe arising separately from the main bronchus and taking over part of the function of the right middle lobe which was diminutive in size.

Case 2. APLASIA OR HYPOPLASIA OF THE LEFT LUNG. Margaret F., aged ten years, weight 50½ lb., suffered from asthmatic bronchitis dating from a severe attack of pneumonia at three-and-a-half months old when she was nursed in a steam tent for four months. Since then she has had pneumonia twice, whooping cough very badly, measles with bronchitis, and ' pleurisy ' twice. She was the third child; the first was still-born and the second died at thirteen days from pemphigus. The father's blood Wassermann reaction had been positive, but became negative one year before the birth of the patient. The mother's Wassermann reaction was

negative, but she had had one miscarriage. Margaret was a full-term child, normal delivery, birth weight 6 lb. 5 oz. After birth she had excessive mucus in the respiratory tract and gasped for breath. The mother stated that she had had no illness, accident, or haemorrhage during pregnancy, but on careful questioning she casually remarked that she had had herpes zoster in the first month.

CLINICAL EXAMINATION. The patient appeared about the size of a child of seven years. The left side of the chest was flatter and smaller than the right, and the apex beat was high in the third intercostal space outside the nipple line. There was no clubbing, and the trachea felt central.

X-RAY OF THE CHEST (fig. 4). The heart was displaced to the left and backward, and the right lung

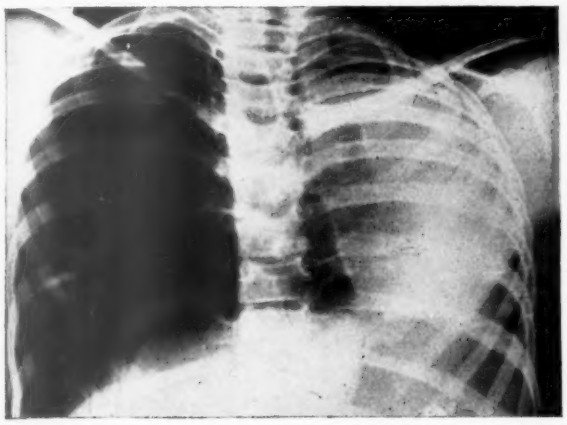

FIG. 4.—Case 2. Aplasia of left lung with herniation of right lung into the left chest.

had herniated through the anterior mediastinum to the left side. There was a calcified lesion in the right lung.

BRONCHOSCOPY. No main bronchus was seen on the left, the first main division was anteroposterior, and each branch then divided again almost immediately into two branches.

BRONCHOGRAM (fig. 5, 6, 7 and 8) revealed a large right bronchial tree with three large branches for the upper lobe probably arising separately from the main trunk, and smaller middle and lower lobe bronchi. The left main bronchus had rotated backward, lying in front of the vertebrae as a single small bronchus dividing in its lower third.

Case 3. HYPOPLASIA OF THE RIGHT LUNG. April K., aged five-and-a-half months, weight 8 lb., was

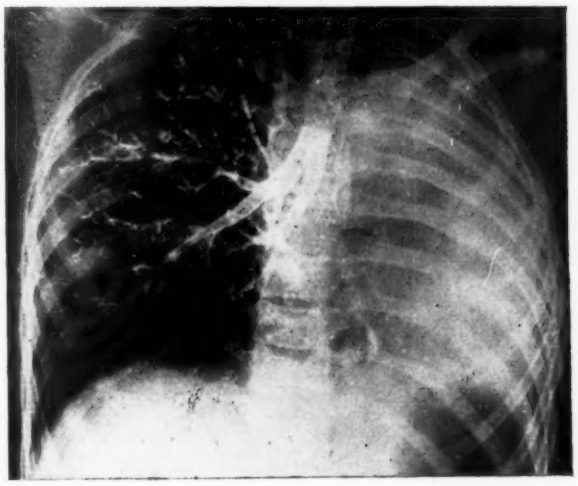

FIG. 5.—Case 2. Bronchogram, A-P view. Left main bronchus is probably the branch overlying the vertebrae. Right bronchial tree enlarged with abnormal branching. (See case report.)

admitted to hospital with the history that she had had bad coughing attacks since birth and was not gaining weight. She was born at full term (face presentation), weighing 5 lb. 4 oz. Oxygen had been required at birth and she had been blue for the first three days. She was breast fed for one month, but gain in weight had always been slow. The parents and two brothers were healthy and there had been no miscarriages, but the mother had nursed her two other boys through pneumonia, chickenpox and measles during the pregnancy.

CLINICAL EXAMINATION. The child was poorly developed and cyanosed with rapid breathing. Temperature 102·8° F., pulse 170, respirations 76 per minute. Examination of the chest revealed no

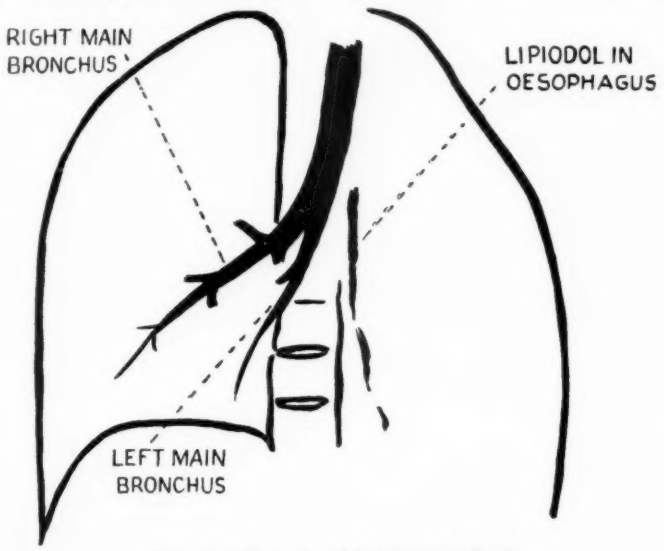

FIG. 6.—Case 2. Diagram of fig. 5.

asymmetry, but the trachea was deviated to the right. There was a hyperresonant note on the left side and dull percussion note on the right, with the maximum apex beat just below the right nipple where a harsh systolic murmur could be heard.

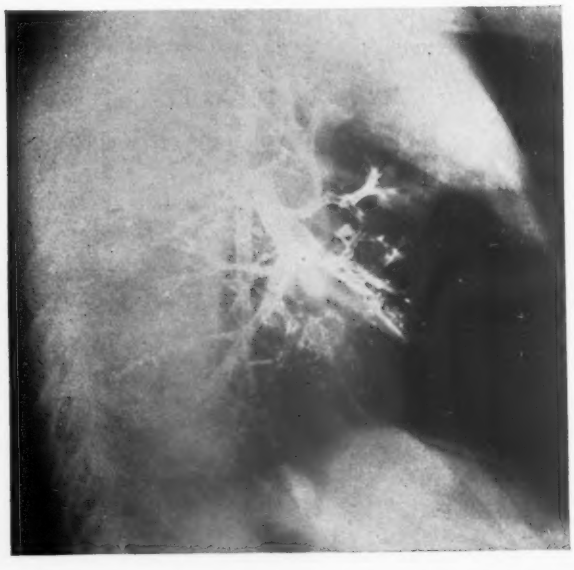

FIG. 7.—Case 2. Right lateral bronchogram. Left main bronchus lies immediately anterior to vertebral bodies and posterior to right main bronchus.

Numerous râles could be heard on the left side, but nothing on the right.

X-RAY OF THE CHEST showed the rib spaces equal on both sides, but the heart was displaced into the right side. The right diaphragm was high and the trachea was deviated to the right. An opacity at the left apex on admission cleared in later films.

BRONCHOGRAM (fig. 9) was performed when the temperature and physical signs had subsided. Only the trachea and main bronchi were filled, but they showed marked curving of the trachea to the right, with slight narrowing before its bifurcation into a large left main bronchus and diminutive right main bronchus sharply bending to the right.

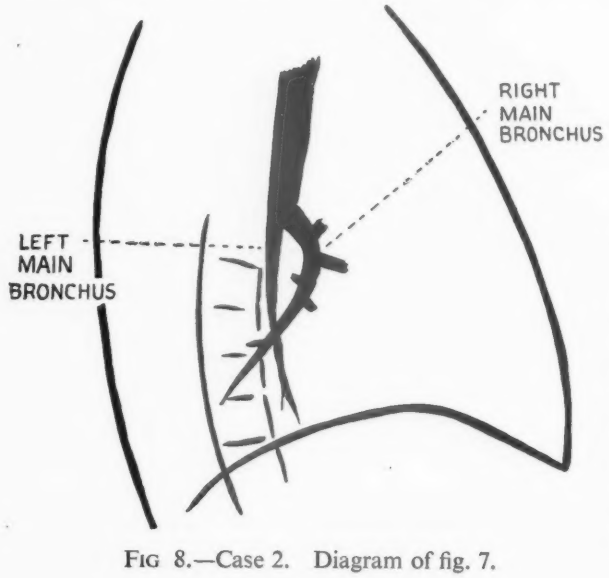

FIG 8.—Case 2. Diagram of fig. 7.

BRONCHOSCOPY. Mr. Crooks recorded that 'the curved trachea straightened out on the bronchoscope so that a bifurcation could be seen. To the right and below was a minute tube leading presumably to the right lung. It expanded and contracted on respiration as would a normal bronchus. It was impossible to say if air came in and out. To the left and above, a larger tube led to the left lung and it was about normal in size and air passed easily through it.'

PROGRESS. After an initial course of sulphamezathine the child's condition improved, the temperature fell to normal and the respirations to 45 per minute. The child was discharged home after a month, still with a few moist sounds in the chest. Two months later she was readmitted as an emergency, having had a cough for one week. She was cyanosed, breathless, wheezing and coughing, and there was swelling of the hands and feet. In spite of oxygen and sulphonamide therapy, she died the following day.

Post-mortem report (fig. 10 and 11) by Dr. M. Bodian. A. K., aged eight months. A wasted, cyanosed infant.

THORAX. Trachea showed deviation to the right.

HEART. A large, quadrangular heart filled the whole of the right thoracic cavity. Both ventricles were hypertrophic; the valves were normal. An interventricular septum defect of about ¼ inch

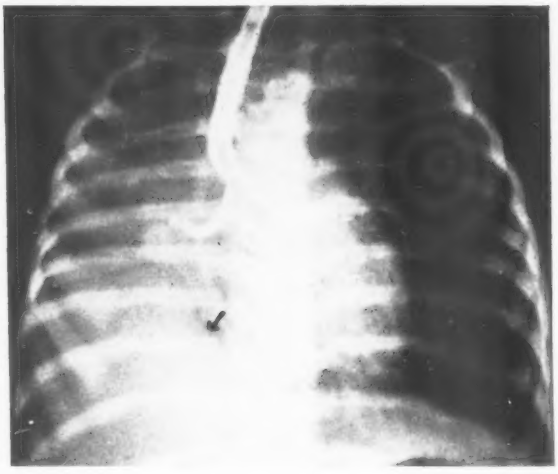

FIG. 9.—Case 3. Bronchogram. Incomplete filling of bronchial tree, showing curving of trachea to the right with large left main bronchus and diminutive right main bronchus. Hypoplasia of right lung. Heart displaced into right chest. Right diaphragm (marked with arrow) is high.

diameter was present at the site of the membranous septum.

LUNGS. Behind the heart and fully covered by it lay a very small hypoplastic right lung which showed no division into lobes. The right main bronchus was much narrower than the left one. The three secondary bronchi were patent throughout, leading to what would normally have been upper, mid- and lower lobes. The lower lobe of the left lung showed marked consolidation and pleurisy.

MENINGES, LIVER, SPLEEN and KIDNEYS were congested. All the other organs appeared to be normal.

Histology of the hypoplastic lung showed no

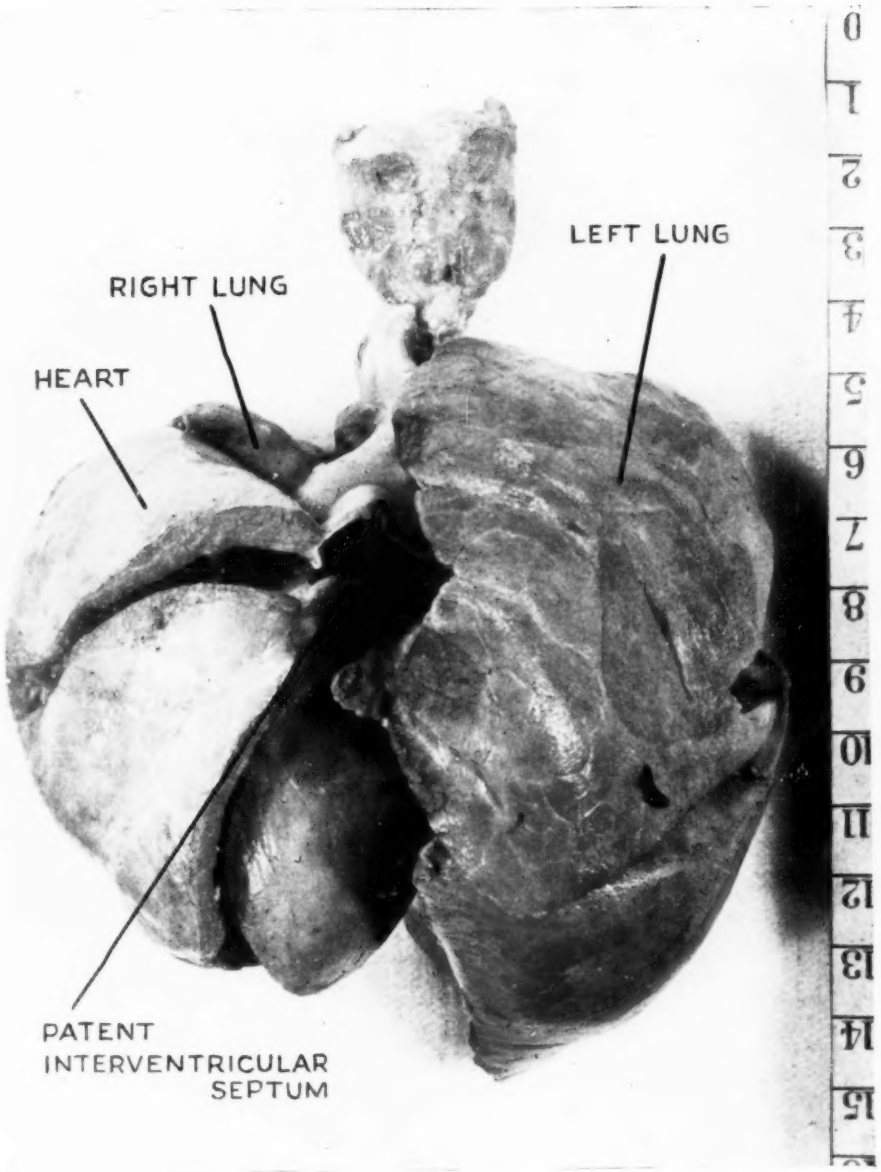

FIG. 10.—Case 3. P.M. specimen, anterior view. Hypoplasia right lung and patent interventricular septum. Right lung behind the heart and hardly visible, left lung enlarged.

proper alveolar formation in most parts. Where laid down, alveoli were primitive and lined by cuboidal epithelium. The bronchioles were of normal appearance.

Case 4. HYPOPLASIA RIGHT LUNG. Alfreda W., aged two years seven months, weighing 20¾ lb., attended hospital for recurrent coughs and colds, which had been worse since pneumonia three months previously. Her birth weight was 4 lb. 12 oz., but she was reported to be full term. Delivery was normal, but her mother had a slight fall when two months pregnant. The infant had been slow in gaining weight since birth. A grandmother had asthma and grandfather died of bronchiectasis. There are three other children, one of which is wheezy.

CLINICAL EXAMINATION. The patient was noticed to be small for her age with a frail appearance. There was some flattening of the right side of her chest and trachea was displaced to the right, but movement was equal on the two sides. The apex beat was felt just to the right of the sternum and percussion note was dull on the right side anteriorly, and also to a less marked degree on the right behind. Faint tubular breath sounds were heard over the right lung, but no adventitious sounds. Later, during an upper respiratory tract infection, however, a unilateral wheeze with rhonchi was heard on the right side. There was no clubbing. The abdominal viscera were not transposed.

X-RAY OF CHEST (fig. 12) revealed the heart situated in the right chest, and the trachea deviated to the right; translucency of the right lung was equal to that of the left. In the lateral x-ray there was a translucent area in front of the heart

displacing it backwards. There has been no change in this picture over a period of four-and-a-half years.

SCREENING OF THE CHEST showed the apex beat in the mid-line just above the xiphisternum and equal translucency of both lung fields. The right lung was displaced posteriorly.

BRONCHOSCOPY. The trachea was found to bend sharply to the right so that the operator's head had to bend well over to the left. There was no stricture of the trachea and nothing abnormal was detected in the bronchial tree.

RIGHT BRONCHOGRAM in 1941 at two years eight months of age and repeated in 1945 (fig. 13) showed small right middle and lower lobe bronchi and a large right upper lobe bronchus with a rudimentary branch arising separately from the right main bronchus.

Case 5. HYPOPLASIA LEFT LUNG. Ronald B., aged six years, weight 39½ lb., first attended hospital for cough five years previously when he was diagnosed as suffering from 'broncho-pneumonia of the left lung with collapse of the left upper lobe.' The cough cleared, but the x-ray appearances persisted. He also had a cleft palate, stenosis of the trachea, congenital deformity of cervical vertebrae (fig. 14) with a torticollis and probably a congenital heart. He had suffered from whooping cough and chickenpox. He was born at full term, weighing 9 lb., and the delivery was normal. The mother had no accident during pregnancy.

CLINICAL EXAMINATION. He was a little undersized for age and showed a marked torticollis to the left with compensatory scoliosis of the thoracic vertebrae which was concave to the right. There was no clubbing and the trachea was central, but movement of the left side of the chest was less than on the right. The apex beat was situated in the fourth intercostal space in the anterior axillary line where a systolic murmur was heard. The percussion note was impaired over the whole of the

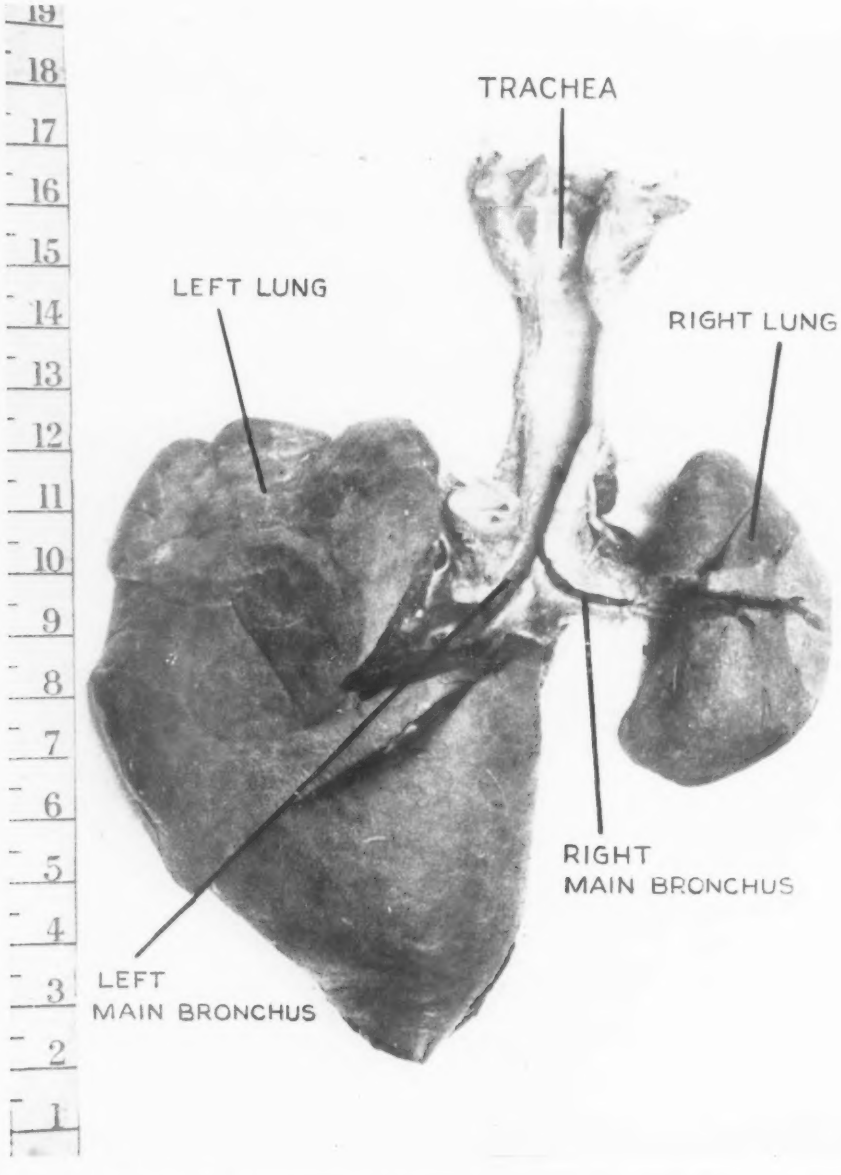

FIG. 11.—Case 3. P.M. specimen, posterior view. Hypoplastic right lung with small bronchus shown in contrast to large left lung and bronchus.

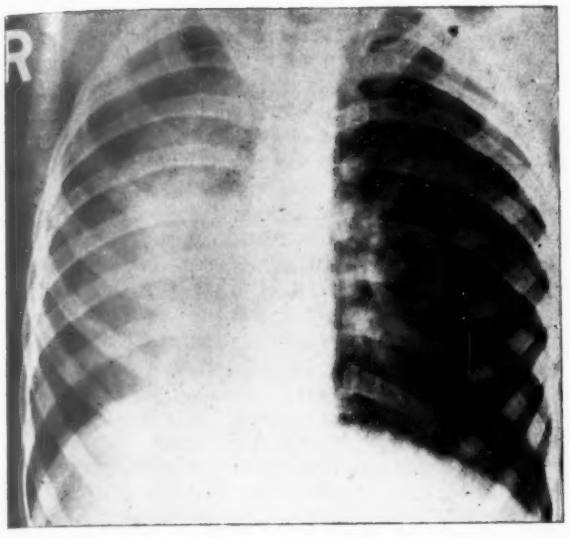

FIG. 12.—Case 4. Hypoplasia of right lung. Heart is situated in the right chest, but translucency of right and left lungs is equal.

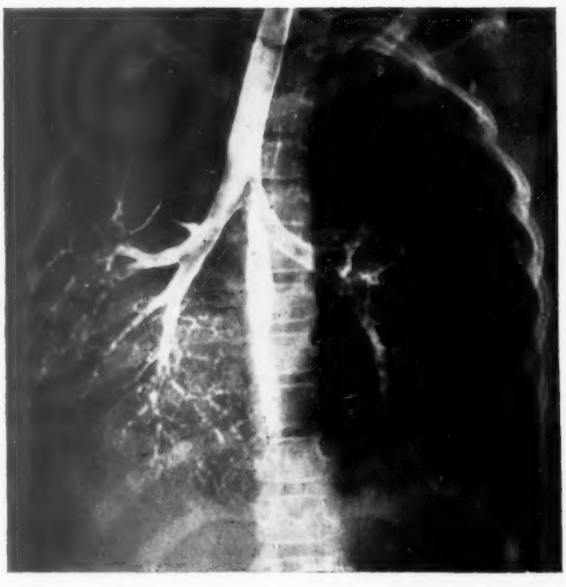

FIG. 13.—Case 4. Right bronchogram, A-P view. Anatomical anomaly of right bronchial tree. (See case report.)

left chest, but air entry was good. Scattered rhonchi, which later cleared, were heard on admission.

X-RAY OF CHEST (fig. 14) showed crowding of the ribs on the left side with displacement of heart to the left and loss of translucency in the left chest. The trachea was slightly displaced to the right. In the lateral view, an area of hypertranslucency extended anteriorly in the superior mediastinum and in front of the heart, which was displaced backwards. There has been no change in this picture for the last four-and-a-half years. The abnormality of the cervical vertebrae and resultant scoliosis make interpretation of this x-ray difficult without further corroboratory evidence.

SCREENING OF THE CHEST. Dr. L. G. Blair reported ' Heart is to the left. Right lung extends across the mid-line. Left lung is emphysematous and the bronchogram agrees with the diagnosis of partial agenesis of the lung.'

BRONCHOSCOPY. There was a definite narrowing towards the lower end of the trachea that was more difficult to pass than the glottis. On withdrawing the bronchoscope, the constriction was seen to be a localized narrowing of normal contour. The trachea appeared to be deviated to the left as the bronchoscope had to be tilted considerably to the right, so stretching the mouth. The right bronchial tree was normal, the left bronchial tree was difficult to approach, but the bronchi appeared smaller than normal.

LEFT BRONCHOGRAM (fig. 15) revealed a small left lung displaced backwards with a long main bronchus. The abnormality of the bronchial tree was difficult to decipher; the upper lobe was small and there appeared to be no lingular bronchus. Permission for a repeat bronchogram has been refused by the parents.

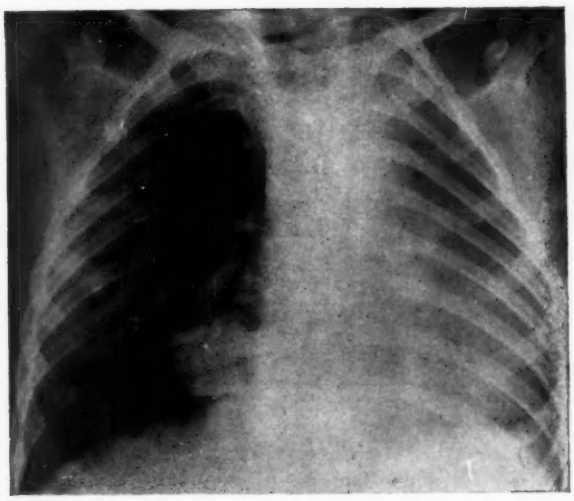

FIG. 14.—Case 5. Hypoplasia of left lung. Heart is displaced to the left. Congenital abnormality of cervical vertebrae produces scoliosis.

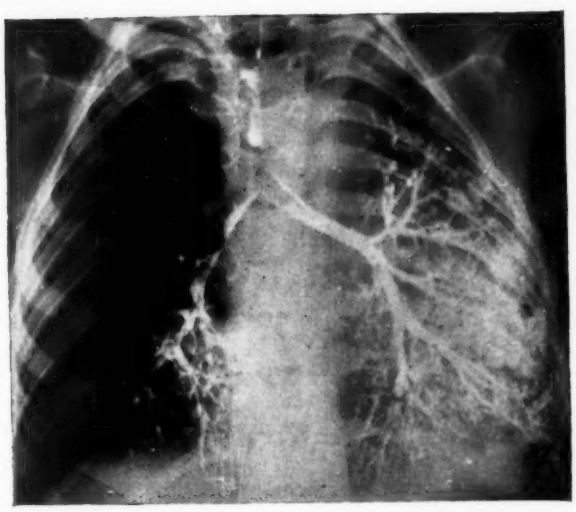

FIG .15.—Case 5. Left bronchogram, A-P view, Anatomical anomaly of left bronchial tree. (See case report.)

Group II

INFANTS IN THE FIRST YEAR OF LIFE SHOWING DISPLACEMENT OF HEART AND MEDIASTINUM WITH SLOW RE-ADJUSTMENT TO NORMAL WITHIN TWO OR THREE YEARS, PROBABLY A TEMPORARY HYPOPLASIA

Case 6. Phyllis W., aged five-and-a-half months, weighing 15 lb. 11 oz., attended hospital for cough at night and occasional vomiting. The mother stated that she contracted whooping cough at three weeks old and measles at four months. She was the third baby (the other children being healthy), was born at full term weighing 8½ lb., and delivery was normal. The mother had no illness, accident or haemorrhage during the pregnancy.

CLINICAL EXAMINATION. She was a healthy, happy, well-nourished child. There was asymmetry of the skull (plagiocephaly) but no scoliosis. The

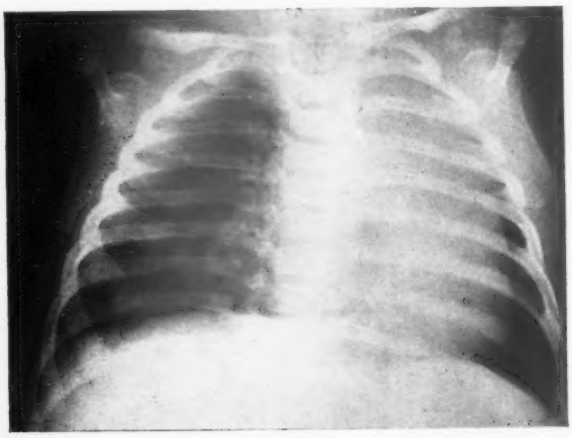

FIG. 16.—Case 6 at five months. Temporary hypoplasia of left lung. Heart is displaced to the left, trachea to the right, but there is hypertranslucency of the left lung.

left chest did not move quite so well as the right. The apex beat was felt in the axilla and there was impaired percussion note at the left apex. Air entry was good on the left side and there were no adventitious sounds.

X-RAY OF CHEST at five months (fig. 16) showed the heart displaced to the left and the trachea to the right, with hypertranslucency of the left lung. Six months later there was still considerable displacement of the heart to the left and a lateral x-ray at this time showed the heart displaced backwards. At the age of two years ten months the heart was more central and in the last x-ray taken at four years two months the heart is practically in its normal position.

SCREENING OF THE CHEST at five-and-a-half months showed a shift of the heart and mediastinum to the left, but no evidence of collapse in the left lung. If pertussis had been the cause of the mediastinal shift, collapse of the left lung, or obstructive emphysema of the right, would have been expected.

BRONCHOSCOPY and BRONCHOGRAM were not performed.

PROGRESS. Apart from a periodic cough associated with naso-pharyngeal infections, the child has kept well.

Case 7. John K., aged five-and-a-half months, weighing 14 lb. 13 oz., attended hospital for shivering and cold for three days, and loss of appetite for one day. There had been no previous illness. He was the second child, born at full term weighing 6 lb. 13 oz., and delivery had been normal. The mother had no illness, accident or haemorrhage during the pregnancy.

CLINICAL EXAMINATION. He also showed an asymmetry of the skull, but no scoliosis. The right side of the chest was flattened particularly in the axilla and the sternum depressed so that the ribs formed a prominent vertical ridge in the nipple line. Clinically, the child presented the picture of pneumonia with temperature 100·4° F. and respiration 63 per minute; the alae nasi were working. The percussion note was impaired all over the right chest with scattered râles and friction at the right base. Rhonchi were heard in both lungs. Following the administration of sulphadiazine, the temperature and respirations fell to normal, the adventitious sounds disappeared from the lungs, but the percussion note remained impaired at the right apex with tubular breathing. Air entry was equal in the two lungs but the deformity of the chest persisted.

X-RAY OF CHEST at five-and-a-half months (fig. 17) showed flattening of the right chest and narrowing of the rib spaces. The heart and mediastinum were displaced to the right, particularly the upper mediastinum which appeared to occupy the right apex. The child was then x-rayed after being tilted to the left, so that the rib ends were equidistant from the centre. In this position it was noted that although the clavicles were not central, the heart was still displaced to the right and there was nothing to suggest collapse of the right upper lobe, the right lung being as translucent as the left. At one year old the displacement of the heart was less marked, and at two years nine months the

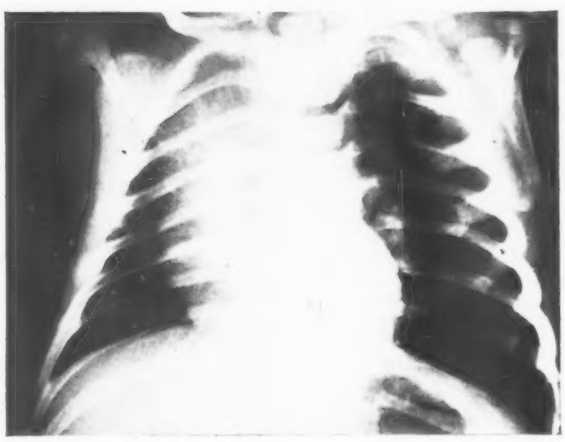

FIG. 17.—Case 7 at 5½ months. Temporary hypoplasia of right lung. There is flattening of the right chest with narrowing of rib spaces. Heart and mediastinum are displaced to the right and occupying the right apex.

heart and mediastinum had returned to their normal position. The early lateral x-rays were too poor for reproduction, but they did show an area of emphysema antero-superiorly, probably an extension of the left upper lobe into the anterior mediastinum.

SCREENING THE CHEST showed the heart and

mediastinum, particularly the superior part, displaced to the right, but there appeared to be full aeration of the right lung, as the translucency was equal to that on the left. There was no evidence of collapse of the right upper lobe.

BRONCHOSCOPY. This was performed two weeks after the onset of pneumonia. The right upper lobe bronchus had a very small opening with thick congested mucosa but no excess secretion. Bubbles appeared at the mouth of the bronchus on respiration, indicating that air was passing. The rest of the bronchial tree was normal.

BRONCHOGRAM was not performed.

PROGRESS. The child has remained quite well since the pneumonia at five-and-a-half months. He has no cough and I am informed that the flattening of the right side soon became imperceptible.

Case 8. Brian W., aged three-and-a-half months, weighing 13 lb. 4 oz., was noticed by the Infant Welfare doctor to hold his head backward and to the right side; this could be corrected without any difficulty or pain to the child and no congenital deformities were detected except in the chest. He was the first child; the delivery was normal, the birth weight 7 lb. 12 oz., there had been no previous illness and no cough. The head posture was easily corrected by the mother carrying the child on the opposite arm.

CLINICAL EXAMINATION. Apart from the posture of the head, there was facial asymmetry and slight

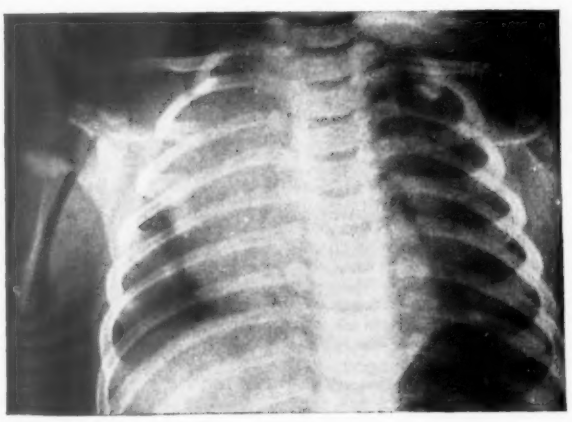

FIG. 18.—Case 8 at seven months. Temporary hypoplasia of right lung. Heart and mediastinum are displaced into the right chest. No flattening of right chest.

scoliosis of the upper thoracic vertebrae which was concave to the right, so that the right chest appeared smaller. The infant was difficult to examine and the borders of the heart were not delineated clinically, but no murmurs were heard. On percussion, the note was emphysematous and the air entry was equal on the two sides.

X-RAY OF CHEST at three-and-a-half months was not central, but at seven months of age (fig. 18) it showed displacement of the heart and mediastinum to the right, particularly in the upper part. The scoliosis was practically corrected and the clavicles were symmetrical, but the line of the costo-chondral junctions was asymmetrical. Serial x-rays over a period of two-and-a-half years showed a gradual return of the heart and mediastinum to the normal position, and fig. 19 reproduces the last x-ray taken at the age of three years.

SCREENING OF THE CHEST demonstrated the displacement of heart and mediastinum to the right. There appeared to be also a separate rounded opacity at the right apex situated anteriorly which did not pulsate but increased in size on crying and diminished in size on inspiration. A superimposed large thymus was suspected. The translucency of right and left lung fields was equal. Further screening at three years of age revealed no abnormality.

BRONCHOSCOPY and BRONCHOGRAM were not performed.

PROGRESS. The child has always been very well. There is now no asymmetry of face or chest.

Case 9. John C., aged ten months, weighing 10 lb. 7 oz., was brought to hospital because he

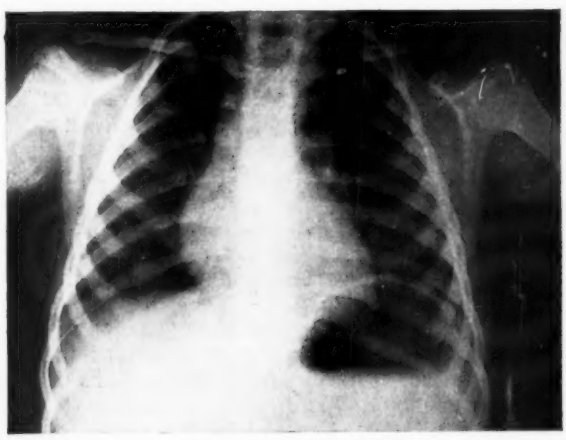

FIG. 19.—Case 8 at three years. Heart is practically in its normal position.

failed to thrive and vomited after most feeds. He was a twin, six weeks premature, the birth weight being 4 lb. His twin sister progressed satisfactorily. There were no previous illnesses. During the pregnancy his mother suffered from anaemia in the early months and had at the end of the fifth month what her doctor termed a precursor to a miscarriage.

CLINICAL EXAMINATION. The infant was wasted and showed a marked asymmetry of the face with prominent veins on the scalp and chest. The fontanelle was large. There was no scoliosis and no flattening of the chest. The apex beat was difficult to define, but there was a diffuse pulsation under and to the right of the sternum. Air entry was equal in the two lungs and there were no adventitious sounds.

X-RAY OF CHEST (fig. 20) showed displacement of heart and mediastinum with the trachea to the right. The translucency of the lung fields was equal, but the line of the costo-chondral junctions was asymmetrical. Lateral x-rays showed an area of emphysema antero-superiorly. Serial x-rays over a period of two-and-a-half years showed a gradual return of the heart and mediastinum to the normal position. The last x-ray was taken at the age of three-and-a-half years, and confirmed the normal position at this time.

SCREENING THE CHEST. The heart and mediastinum were displaced to the right and the maximum

impulse (apex beat) was on the left border of the heart. Both lungs aerated equally.

BARIUM SWALLOW revealed a congenitally short oesophagus with stricture.

BRONCHOSCOPY and BRONCHOGRAM were not performed.

PROGRESS. After a very difficult period when he developed gastro-enteritis, the patient made a slow but steady improvement. He has now almost reached normal weight for age. He vomits only occasionally and the asymmetry of the face is less noticeable.

Case 10. Roy G., aged nine months, weighing 21 lb. 3 oz., was admitted to hospital for repair of harelip. Following the operation he developed a cough and was therefore x-rayed. He had clinical and x-ray evidence of rickets with bossing of the head, but there was no asymmetry of head or chest. He was the fifth child and there were no previous illnesses.

X-RAY OF THE CHEST at nine months of age (fig. 21) showed the heart, trachea and mediastinum displaced to the right with a rounded shadow at the right hilum, probably the thymus. The last x-ray taken at eighteen months of age showed slight improvement in the position of the heart and disappearance of the rounded opacity.

SCREENING THE CHEST. The heart and mediastinum were displaced to the right, and aeration of the two lungs was equal. The rounded opacity was difficult to define.

PROGRESS. At ten months he contracted whooping cough and developed pneumonia, but had fully recovered when last seen at eighteen months of age, when he had no cough.

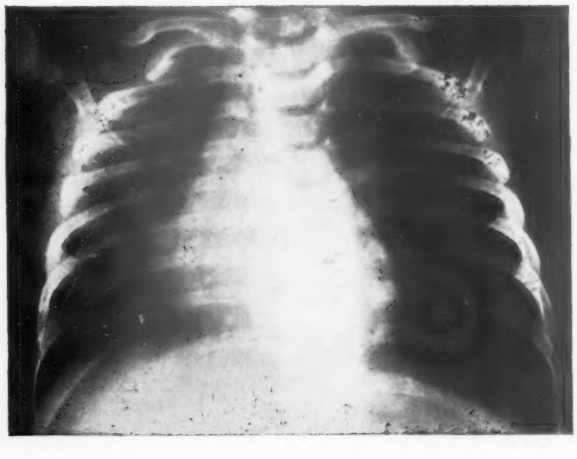

FIG. 20.—Case 9 at ten months. Temporary hypoplasia of right lung. Heart and mediastinum with trachea are displaced to the right.

Case 11. Christopher K., aged ten weeks, was admitted to hospital in a dyspnoeic state with attacks of cyanosis which he had had since birth. He was the fourth child, and was one of twins; the other twin was a miscarriage at the third month of pregnancy. Christopher was a full term child; the delivery was normal, and the birth weight 7 lb. 12 oz. The mother had no illness or accident apart from the miscarriage during the pregnancy. There was no cough.

CLINICAL EXAMINATION. He was a sickly infant, cyanosed, dyspnoeic and sweating. He had a cleft palate with a severe degree of micrognathia causing respiratory stridor. There was no asymmetry of the head or chest, but the latter showed inspiratory recession of the intercostal spaces and ribs with pigeon deformity.

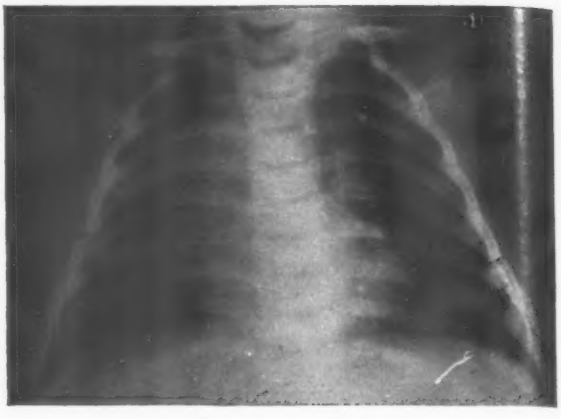

FIG. 21.—Case 10 at nine months. Temporary hypoplasia of right lung. Heart, mediastinum and trachea are displaced to the right. Rounded opacity at right hilum is probably thymus.

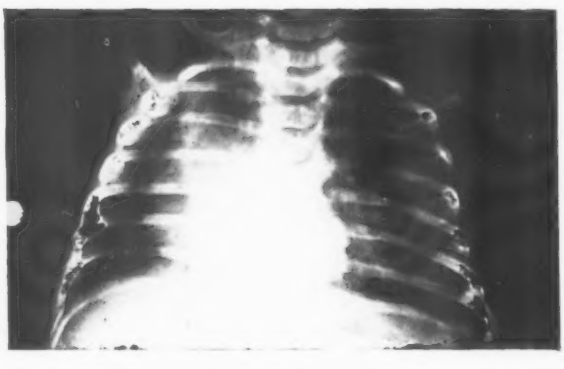

FIG. 22.—Case 11 at 2½ months. Temporary hypoplasia of right lung. Child is slightly rotated to the right. Heart and mediastinum are displaced to the right with herniation of left lung into the right chest. Trachea is central.

X-RAY OF CHEST (fig. 22). At the age of two-and-a-half months, x-rays were taken in three positions, viz. a little to the right, central and a little to the left, and in all it was observed that the heart and mediastinum were displaced to the right: the trachea, however, was central. A lateral x-ray showed a strip of emphysema anteriorly with displacement of the heart backward.

SCREENING THE CHEST. Dr. L. G. Blair reported: 'The heart is definitely and permanently displaced to the right, ? due to collapse of a portion of the lung, although I cannot see any lung so collapsed, ? partial agenesis. There is some consolidation in the right mid-zone.'

PROGRESS. At first the infant's condition improved, but he was readmitted suffering with gastro-enteritis, and although he recovered from this, he finally died at the age of four months from measles and broncho-pneumonia. Unfortunately he was admitted to, and died in, a fever hospital without details of his former history being available; no post mortem was performed.

Group III

INFANTS WITH A LOCALIZED TRIANGULAR OPACITY IN THE X-RAY

(It is suggested that this might be caused by hypoplasia or atelectasis of part of a lung with no bronchial communication.)

Case 12. Garry W., aged two years and four months, weighing 29 lb., was admitted to hospital for second-stage cleft palate operation and was x-rayed because he had a cough; this had persisted since whooping cough twenty-one months previously. He was born at full term, weighing 8 lb., and delivery was normal. When two to three months pregnant his mother had a bad fall downstairs. There was one other child in the family, who was healthy.

CLINICAL EXAMINATION. The child looked well and there were no abnormal physical signs in the chest. The Mantoux tuberculin test 1 in 1,000 was negative.

X-RAY OF THE CHEST at two years and four months (fig. 23 and 24) showed a triangular shadow in the upper mediastinum on the right side with a concave outer margin. In the oblique and lateral positions (fig. 25 and 26) this opacity takes the shape of a collapse of the pectoral part of the right upper lobe. There is also a small hernia of the right diaphragm. Serial x-rays taken over a period of two years show the shadow comparatively, but not actually, smaller.

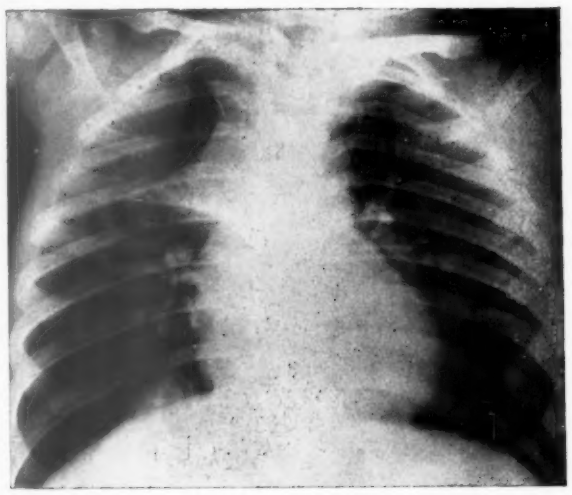

FIG. 23.—Case 12 (A-P view). ?Hypoplasia of part of right upper lobe. A triangular opacity in the right upper mediastinum is seen with a small hernia of the right diaphragm.

FIG. 24.—Case 12. Diagram of fig. 23.

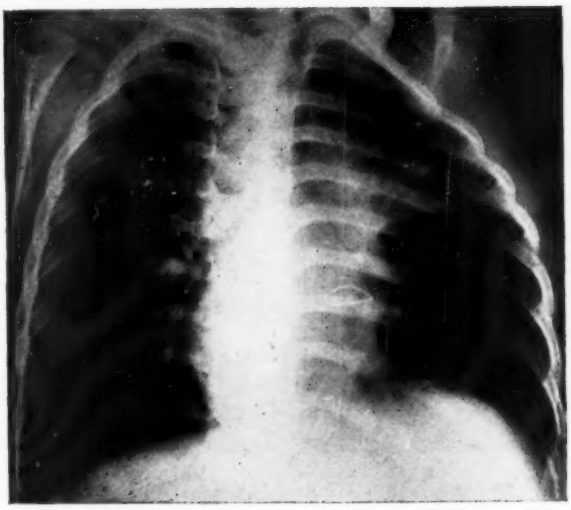

FIG. 25.—Case 12 (right oblique position). The triangular opacity is visible in the right upper lobe area.

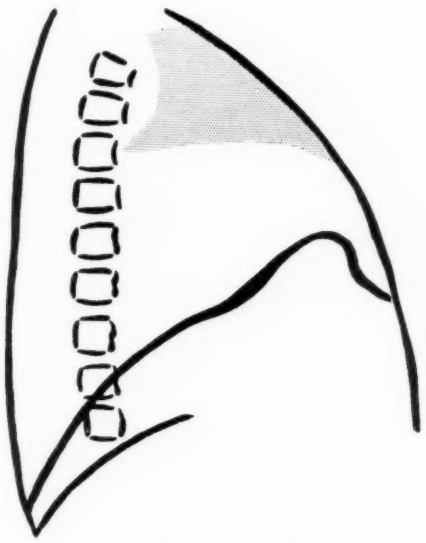

FIG. 26.—Case 12. Diagram of right lateral position. The triangular opacity is occupying the usual position of the pectoral segment.

SCREENING showed that the opacity was situated anteriorly and limited below by the lesser fissure. It diminished in size on inspiration and enlarged on expiration.

BRONCHOSCOPY. The right main bronchus was very small with loose puckered mucosa and the bronchoscope would not pass. The left bronchial tree appeared normal.

RIGHT BRONCHOGRAM (figs. 27, 28, 29, and 30) revealed two narrowings of the right main bronchus before its first division. There appeared to be no bronchus entering the triangular opacity. A repeat of the bronchogram at four years eight months still revealed no bronchus entering the opaque area.

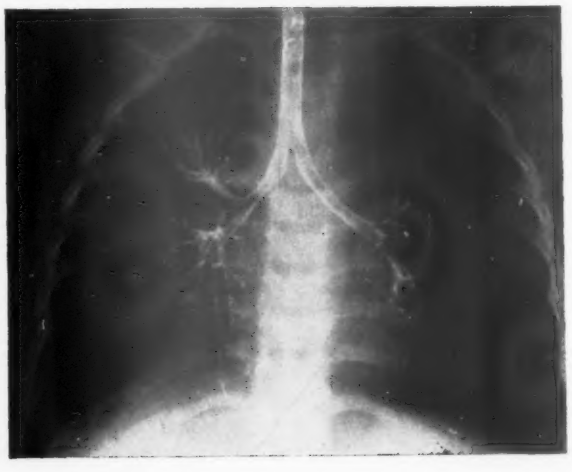

FIG. 27.—Case 12 (right bronchogram, A-P view). No bronchus enters the triangular opacity. There is a double stricture of the right main bronchus.

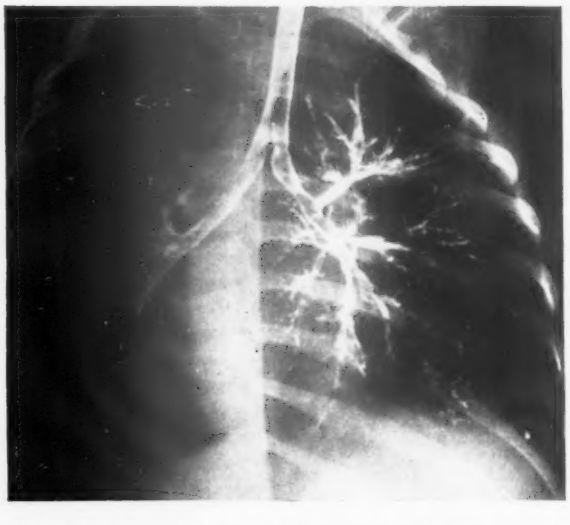

FIG. 28.—Case 12 (right bronchogram in oblique position). The double stricture of right main bronchus is clearly visible. Anatomical position of the bronchi not helpful in this position.

PROGRESS. Apart from intermittent colds and coughs the child is making satisfactory progress and is overweight for age.

Case 13. Sidney C., aged five months, was first brought to hospital because he had been chesty since 2 months old. He was the third child, born full term, normal delivery, birth weight 7½ lb. There had been no previous illnesses. His mother had no illness, accident or haemorrhage during the pregnancy.

CLINICAL EXAMINATION. The breathing was partially obstructed and breath sounds were harsh in character. There were no adventitious sounds. The tuberculin patch test was negative.

X-RAY OF THE CHEST at five months (fig. 31 and 32) showed a triangular shadow in the right upper mediastinum with convex borders. It was difficult to define the shadow in the lateral x-ray, but it appeared to be anterior in the oblique (fig. 33). The last x-ray taken at two years and two months showed little change.

SCREENING THE CHEST. Dr. L. G. Blair reported: 'The opacity, spreading out into the right lung, is situated anteriorly, and I think is probably due to collapse of portion of the upper lobe.' It was observed to diminish in size on inspiration and enlarge on expiration.

BRONCHOSCOPY. No abnormality was detected in the bronchial tree.

PROGRESS. At one year and four months the child contracted whooping cough. At two years and two months the child had no cough but was backward in talking and was rolling his head; low-grade mentality was suspected.

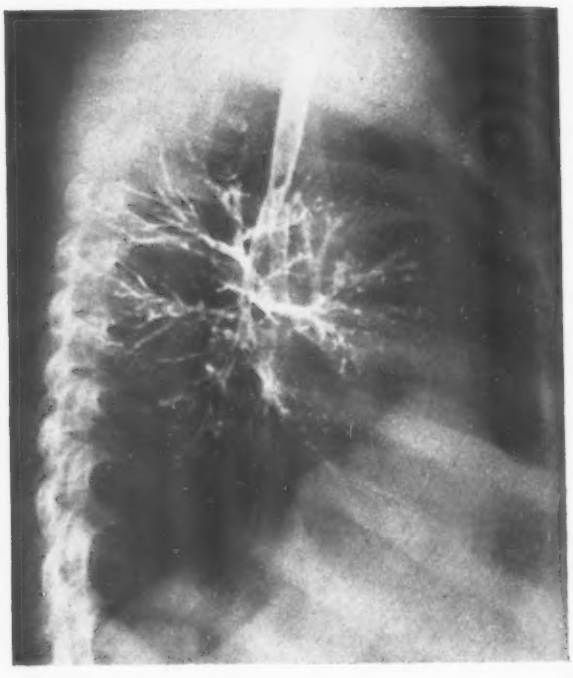

FIG. 29.—Case 12 (right bronchogram in lateral position. There is some filling in the opposite side). No bronchus appears to supply the triangular opacity.

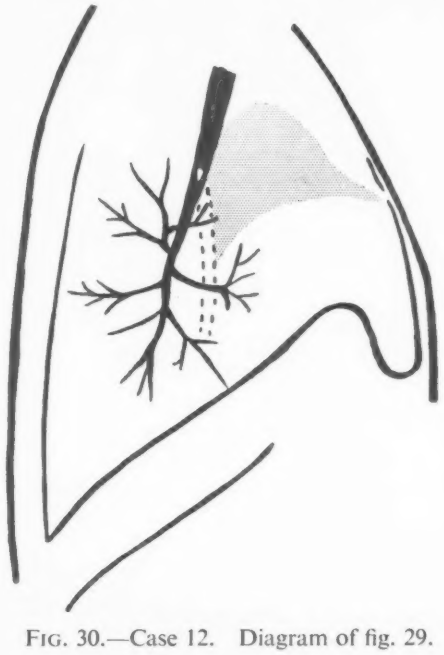

FIG. 30.—Case 12. Diagram of fig. 29.

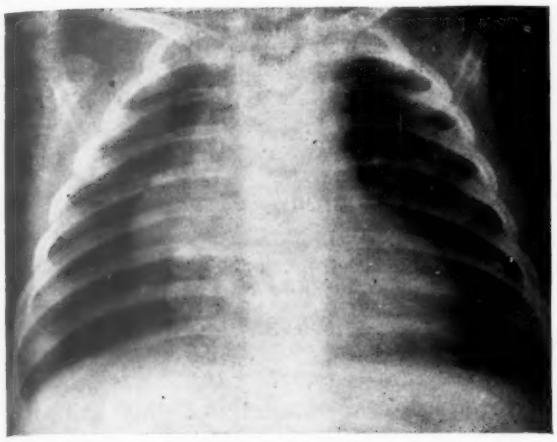

FIG. 31.—Case 13. There is a triangular opacity in the right upper mediastinum. ? Hypoplasia of part of right upper lobe. ? Thymus.

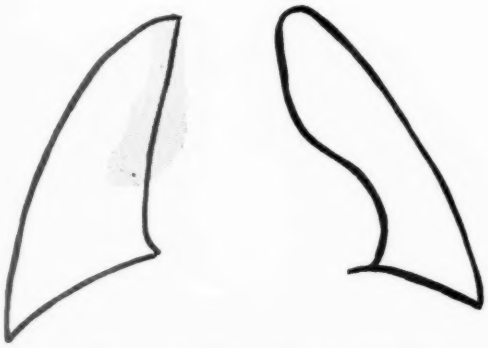

FIG. 32.—Case 13. Diagram of fig. 31.

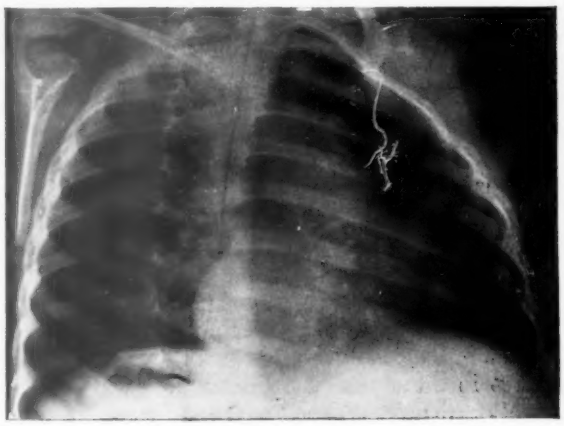

FIG. 33.—Case 13 (right oblique position). The triangular opacity is faintly visible anterior to the cardiac shadow.

Case 14. Keith M., aged eight months, weighing 16 lb. 7 oz., was stated to have had some cyanosis for a few weeks after birth. He was then well and free from cough until three months old when he had an attack of wheezing. This had been repeated two or three times since then. On one occasion rales were heard at the right apex. During one of these attacks he ran a temperature up to 102° F. and respirations rose to 60 per minute; a course of sulphathiazole had little effect. Tuberculin Mantoux test 1 in 1,000 was negative. He is the ninth child, two weeks premature, born normal delivery, weighing 5 lb. 14 oz. His mother had influenza when three to four months pregnant, with high temperature and cough.

CLINICAL EXAMINATION. He was a little backward for his age but otherwise looked normal. There were no abnormal physical signs in the chest.

X-RAY OF THE CHEST (fig. 35 and 36) showed a triangular opacity at the right hilum with straight margins and pointed apex. At one year of age this showed no change, but at seventeen months the opacity had practically disappeared into the mediastinum.

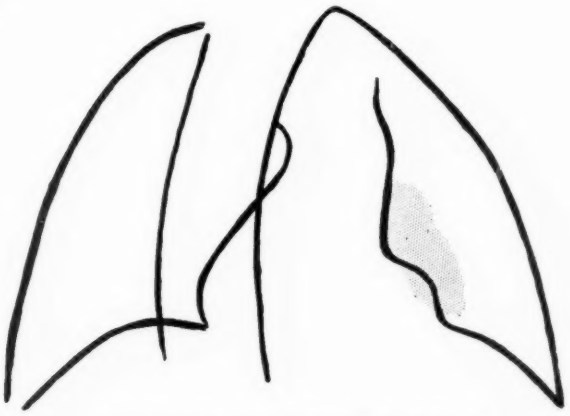

FIG. 34.—Case 13. Diagram of fig. 33.

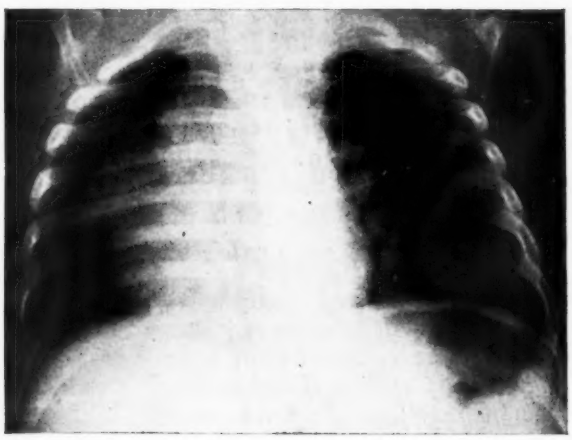

FIG. 35.—Case 14. There is a triangular opacity in the right upper mediastinum. ? Hypoplasia of part of the right upper lobe. ? Thymus.

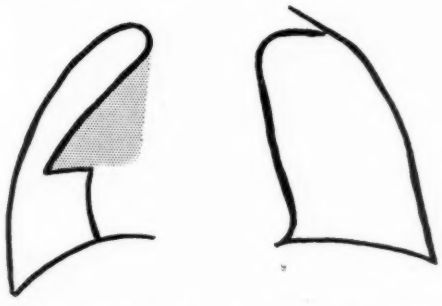

FIG. 36.—Case 14. Diagram of fig. 35.

SCREENING OF THE CHEST was unfortunately not done until the age of seventeen months when the opacity could not be defined.

PROGRESS. At the age of seventeen months the child was well, had no cough and was gaining satisfactorily.

Discussion

The fourteen cases reported here have been recorded because of their rarity, and because diagnosis of maldevelopment of a lung is an important differentiation from atelectasis or pulmonary collapse.

Cases in Group I present a fairly definite diagnosis. In Group II the clinical observation is recorded as such with only suggested explanations of the condition. In Group III the cases are curiosities still undiagnosed, but are recorded in order to encourage others to investigate similar cases, particularly autopsy material if this becomes available.

GROUP I. Cases 1, 2 and 3 showed absence or gross hypoplasia of one lung, but cases 4 and 5 are rare in that there was only partial underdevelopment of one lung. Diagnosis is dependent on a permanent displacement of the heart and mediastinum with equal aeration and translucency of the two lungs, and on an abnormality in the branching of the bronchial tree on the affected side as seen in a bronchogram. No symptoms were produced by the defect and there were no adventitious sounds heard in the chest, as would be expected in a chronic collapse of the lung. All four cases were undersized and cases 1 and 5 showed other multiple congenital abnormalities. Chest deformity with flattening was observed in cases 2, 4 and 5, but the trachea felt central in cases 1, 2 and 5. Screening of the chest was a useful subsidiary investigation.

GROUP II. Cases 6 to 11 comprise a series of radiological observations showing displacement of the heart and mediastinum with nothing to suggest disease or collapse of the lungs. In five cases the displacement was to the right and in one to the left. The translucency and aeration of the two lungs were equal and there were no abnormal physical signs in the lungs. The condition is probably more common than is realized, as few symptoms are produced unless by an associated congenital defect, so that these patients are unlikely to be x-rayed. In addition, these cases were all diagnosed in the first year of life and the displaced heart and mediastinum gradually returned to normal within two or three years.

Whilst reviewing the notes of these cases, it was discovered that several associated congenital anomalies were common to more than one case. Cases 6, 7, 8 and 9 had a definite asymmetry of the head or face, flattening on one side and prominence on the other, but unfortunately the side of the flattening was not recorded and the condition has by now improved or disappeared in most of them. Case 10 had a harelip and case 11 micrognathia and cleft palate. Cases 7 and 8 showed flattening of the chest on the affected side, but only case 8 had a temporary scoliosis. Case 9 had an associated congenital short oesophagus. It will be noted that no case was without an associated congenital anomaly of head or face. This is an important observation in view of the well-recorded fact that in agenesis or hypoplasia of a lung there is commonly associated other congenital abnormalities, and cases 1 and 5 of Group I support this observation. Embryological study reveals the fact that the lung bud appears about the same time as the last pharyngeal pouch and is at first closely associated with development of the face and head. It is not unreasonable, therefore, to suggest that in the cases included in Group II there has been a disturbance in early foetal life causing partial arrest of growth on one side of head, face and chest, including the lung which has corrected itself after birth during growth of the child.

Other radiological possibilities must be considered, such as defective posture producing an apparent displacement of the mediastinum, but

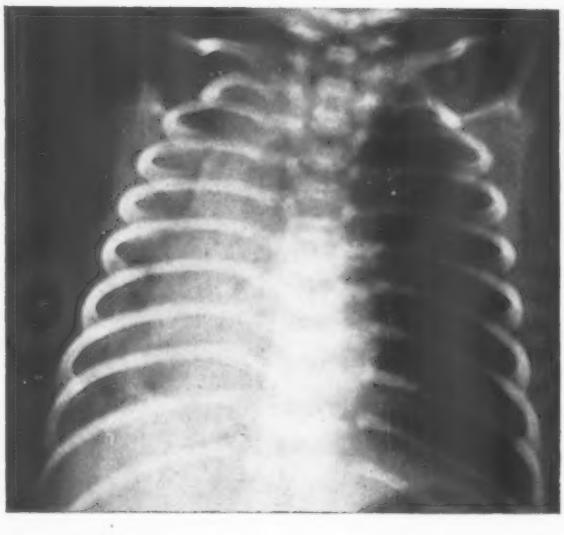

FIG. 37.—Atelectasis of right lung in a new-born baby. Right lung shows loss of translucency.

personal observation whilst screening the child does not support this suggestion. Atelectasis or collapse of the lung would produce loss of translucency and poor aeration (fig. 37) with impaired percussion note on the affected side, and this was not the case. It would have been interesting to see bronchographic pictures in these cases to know whether there was any abnormality of the bronchial tree, but the operation is not without risk in such small infants and it was not felt a justifiable investigation.

GROUP III. Cases 12, 13 and 14 all presented a triangular shadow in the x-ray situated in the right upper mediastinum anteriorly. In case 12, this gave the appearance of a collapse of the pectoral portion of the right upper lobe, but there were no symptoms or physical signs suggesting this diagnosis. (In my experience, atelectasis or collapse of a lung due to acquired pulmonary disease usually becomes infected within a year, producing cough, adventitious sounds in the chest and bronchiectasis unless

re-expansion has occurred.) The bronchograms in case 12 (fig. 19 and 20) suggested that there was no bronchus supplying the opaque area and the phenomena observed on screening the chest make it improbable that air was entering that portion of the lung. In addition, case 12 shows other congenital abnormalities, viz. stenosis of the right bronchus, a small diaphragmatic hernia, and harelip, and case 13 is thought to be mentally backward. During operations on the chest isolated portions of lung tissue have been found in the mediastinum in the region of the lower lobe which did not communicate with a bronchus (personal communication, Dr. L. G. Blair), and it is suggested that the opacities seen in the x-rays of Group III are of this nature. Further observation, with bronchograms and autopsy material, will be necessary to elucidate the problem.

AETIOLOGY. In an attempt to correlate congenital anomalies in the lung with intra-uterine disturbance, a questionnaire was sent to all the mothers of the above patients asking for information on the birth of the child, as well as the occurrence of any illness, accident or haemorrhage during the pregnancy, and if so, at what stage. The answers were interesting.

In Group I, the mother of case 1 had a bad fall when two months pregnant, and the mother of case 4 a slight fall at two months. The mother of case 2 had herpes zoster in the first month of pregnancy.

In Group II, the mother of case 9 had a threatened miscarriage at five months whilst carrying twins, and the mother of case 11 had a miscarriage of the twin at three months; the patient was born at full term but had other congenital abnormalities.

In Group III, the mother of case 12 fell downstairs when two or three months pregnant; and the mother of case 14 had influenza and high temperature and cough at three to four months. Although the questionnaire asked for mishaps during the whole of the period of pregnancy, only such occurrences during the first five months were mentioned in the replies, whilst in Group I the first two months (the period of development of the lung buds) was specifically mentioned. The numbers are too small to permit any conclusions to be made, but these findings justify further research into the relationship of congenital abnormalities with mishaps during pregnancy, comparing the results with a control series.

Summary

The fourteen cases reported here fall into three categories.

Group I. Five cases of permanent underdevelopment of one lung.

Group II. Six cases of displacement of the heart and mediastinum in the first year of life, correcting itself within two to three years. It is suggested that this may be caused by a temporary hypoplasia of the lung.

Group III. Three cases showing a triangular mediastinal opacity in the x-ray. The possibility of this being caused by an isolated portion of lung tissue with no bronchial communication is discussed.

Thanks are due to Dr. W. G. Wyllie, the Hospital for Sick Children, Great Ormond Street, for permission to study his cases and for much helpful advice and criticism; also to Dr. W. Sheldon for permission to publish case 3. I am indebted to Dr. M. E. Lund and Dr. M. Ungar for their help whilst working as part-time assistants to the Medical Research Council, also to the Medical Research Council for a grant for expenses.

REFERENCES

Deweese, E. R., and Howard, J. C. (1944). *Radiology*, **42**, 389.

Finkelstein, H. (1924). Lehrbuch der Säuglingskrankheiten. Berlin.

Hurwitz, S., and Stephens, H. B. (1937). *Amer. J. Med. Sci.*, **193**, 81.

Kiebel, F., and Mall, F. P. (1912). Embryology of the Lung, **2**, London.

Killingsworth, W. P., and Hibbs, W. G. (1939). *Amer. J. Dis. Child.*, **58**, 571.

Schneider, P. (1912). In Schwalbe, E., Die Morphologie der Missbildungen des Menschen and der Tiere, **3**, Pt. 2, 817. Jena.

Schwalbe, E. (1912). *Ibid.*, 763.

A FATAL CASE OF BERIBERI IN A CHILD IN ENGLAND

BY

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(From the Children's Hospital, Birmingham)

Beriberi is rarely observed in England. From time to time sporadic cases appear in adults. Jones and Bramwell (1939), Konstam and Sinclair (1940) and others have reported cases due to alcoholism. Bates (1941) recorded the disease in a young woman who neglected herself. Even on the continent, Pyke (1945) in Vienna, and Ellis (1945) in Brussels make no mention of beriberi having occurred during the enemy occupation, though famine oedema appeared in adults and to a less extent in children. The precedence, in nutritional deficiency in Europe, of oedema over beriberi fits in with what has been observed in Birmingham and is to be seen in this case. The probable explanation is that vegetables and bread are relatively richer in thiamin than in protein.

That a child should die of beriberi in England is sufficiently uncommon to warrant publication. Apart from the rarity, the present case presents some unusual findings. Although chronic, with histologically demonstrable changes in the nervous system, the main clinical features were due to the involvement of the heart. The latter showed in the post-mortem examination such changes as would be expected if a typically acute beriberi heart as described by Wenckebach (1934) were to survive for a longer period.

Case report

B. P., born February 15, 1941, was originally admitted to the Children's Hospital, Birmingham, on February 14, 1944 with the following history.

He was the youngest of a family of three of whom the eldest died in infancy of bronchopneumonia, the second having congenital heart disease. The parents were healthy.

Feeding had been by the breast until the age of fourteen months. Since then the diet had contained nearly a pint of milk daily, three to four eggs a week, but neither meat, fish nor greens. After weaning, a teaspoon of cod-liver oil was given in the morning and a cup of orange juice at night. Walking commenced at eleven months and talking five months later.

His teeth were cut 'with bronchitis,' since when he had been subject to a cough. Apart from measles when a year old his general health had remained satisfactory until two weeks before admission when he developed diarrhoea. Two days before coming into hospital the legs and feet became swollen, stiff and painful.

On admission he was seen to be a broad-featured, sallow non-toxic child. The hands were podgy, the feet and legs oedematous. Chvostek's sign was present. There were no other abnormal signs. The urine was normal.

Blood analysis on February 17, 1944, gave the following figures:—

Urea	26	mg. per 100 ml.
Cholesterol	60	mg. per 100 ml.
Calcium	6·1	mg. per 100 ml.
Phosphorus	3·4	mg. per 100 ml.
Albumen	1·53	g. per 100 ml.
Globulin	1·25	g. per 100 ml.
Fibrinogen	0·49	g. per 100 ml.
Pyruvic Acid	1·8	mg. per 100 ml.
Phosphatase	9·2	mg. of P. liberated by 100 ml. of serum in 3 hours at 37 C.

The case was considered to be one of nutritional deficiency aggravated by the diarrhoea. He was given an ordinary diet supplemented by calcium chloride, thiamin, iron and vitamin D. The oedema gradually disappeared. On March 24, 1944, the plasma proteins were:—

Albumen, 3·32; globulin, 2·17; fibrinogen, 0·34 g. per 100 ml.

He was discharged with advice as to diet which now contained an egg every day as well as a pint of milk, but he still did not take either meat, fish or greens. Marmite was given as a vitamin B supplement. He was well and symptom-free, apart from his chronic cough, for four months when the feet began to ache and swell. He remained active for a further four days, then became quiet, and was admitted to hospital the following day (July 25, 1944).

He now looked exhausted, and was orthopnoeic with grunting respiration and a loose cough. The legs and abdominal wall were oedematous, and the liver enlarged to a distance of three fingers' breadths below the costal margin. In the chest were signs of an asthmatical bronchitis which tended to obscure the heart sounds. The apex beat was not palpable, the pulse was 120, feeble and irregular. The heart sounds were very soft. The tendon reflexes were obtained with difficulty. Blood analysis on July 26, 1944 gave the following figures:—

Albumen	2·22	g. per 100 ml.
Globulin	0·90	g. per 100 ml.
Fibrinogen	0·36	g. per 100 ml.
Calcium	9·10	mg. per 100 ml.
Phosphorus	4·50	mg. per 100 ml.
Pyruvic Acid	1·97	mg. per 100 ml.

An electrocardiogram taken on admission (fig. 1)

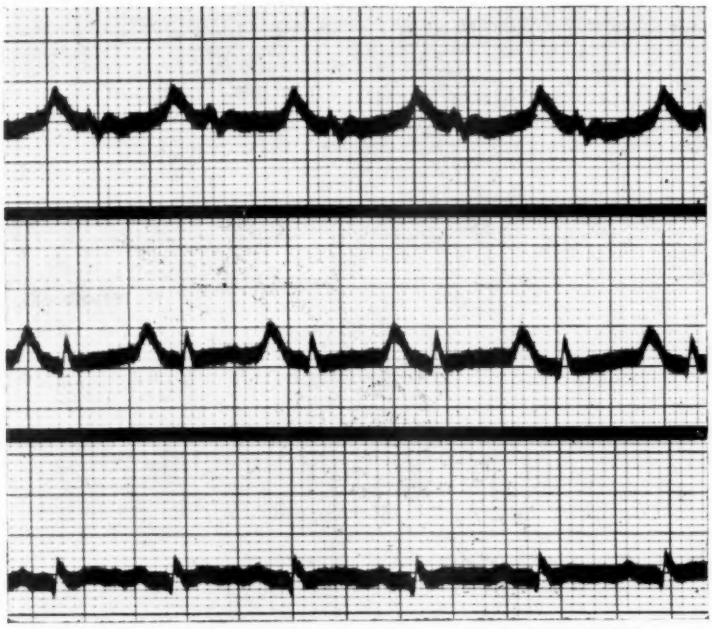

FIG. 1.—Electrocardiogram showing large P waves, low voltage QRS and absent T waves.

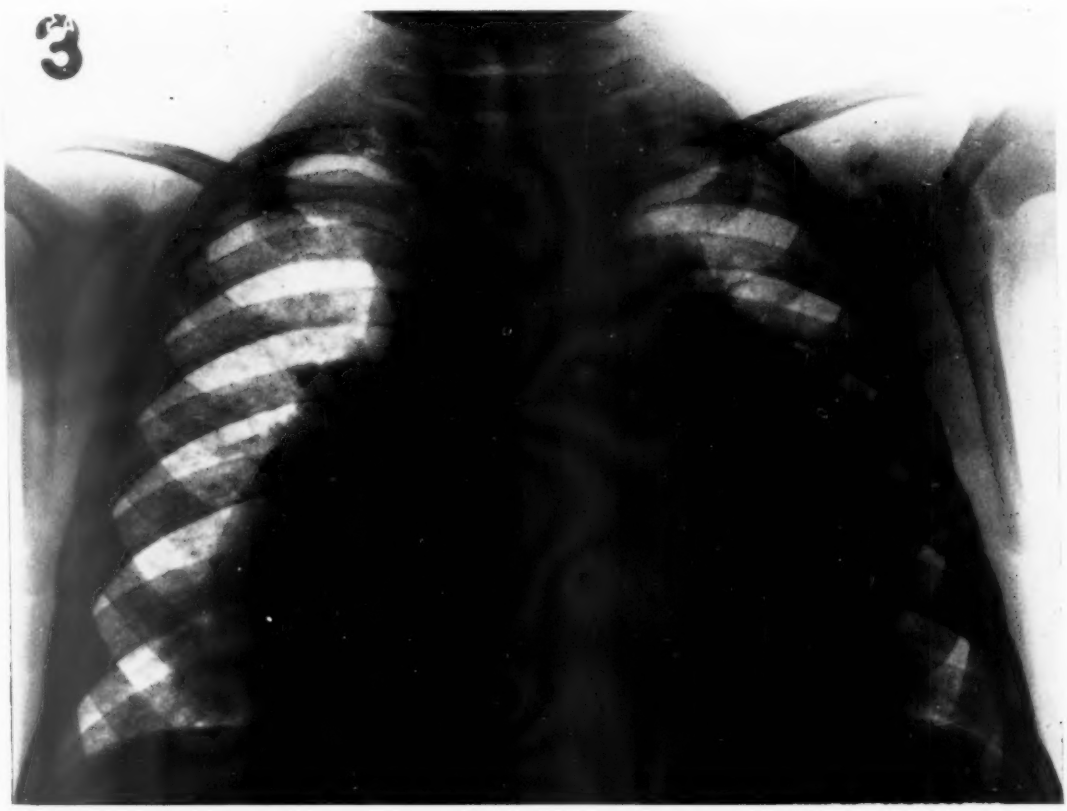

FIG. 2.—Postero-anterior radiograph of the thorax showing right-sided dilatation of the heart.

recorded sinus rhythm which was regular, P 1 and 2 were huge, PR interval 0·18 sec., QRS had a very low voltage and T was flat in all leads. In view of the possibility of beriberi, 2·5 mg. thiamin was given by intramuscular injection every four hours, five times a day. The blood pyruvic acid started to fall within twenty-four hours:—

July 28, 1944, 9.15 a.m., pyruvic acid, 1·13 mg. per 100 ml.

July 28, 1944, 4.0 p.m., pyruvic acid, 1·23 mg. per 100 ml.

July 31, 1944, 10.45 a.m., pyruvic acid, 0·70 mg. per 100 ml.

An x-ray of the chest on July 28, 1944, showed a very large cardiac shadow, the shape being consistent with a pericardial effusion (fig. 2).

The oedema and distress gradually increased. Although he had remained afebrile, in view of the

very large heart shadow the pericardium was tapped on July 31, 1944, but only 60 ml. of a turbid yellow fluid were obtained from which pneumococci and K. Friedländer were subsequently cultured. The boy died the next day.

Morbid anatomy. The body was that of a normally developed, moderately nourished, pale boy. There was oedema of feet, ankles and calves.

The tonsils were the size of lentils and without evidence of inflammation. The larynx, trachea and oesophagus were normal. The cervical lymph nodes were not enlarged. The thyroid was normal in size and appearance. The thymus was atrophic. Each pleural cavity contained about two ounces of clear, straw-coloured fluid. The parietal and visceral pleurae were thin, smooth and lustrous. Both lungs were moderately hyperaemic. On section some muco-purulent exudate was seen in the smaller bronchi but no consolidation was present. The paratracheal and tracheo-bronchial lymph nodes ranged in size from a hemp seed to a pea, were somewhat firm in consistency and dark red in colour. In none was there any evidence of tuberculosis.

The pericardium contained about 2 to 3 oz. (75 c.c.) of fibrino-purulent exudate. The heart was very considerably enlarged, due mainly to a dilatation of the right auricle and ventricle which were grossly distended by dark blood. The weight of the empty heart was 125 g. The wall of the right ventricle was very thin, 1 to 2 mm. in thickness, that of the left ventricle 5 to 8 mm., that of the right auricle 1 to 3 mm. and of the left auricle 1 to 1·5 mm. in thickness. The endocardium of the right auricle and ventricle was thick and milky in appearance (fig. 3). The trabeculae carneae of the right ventricle were extremely flattened. The myocardium of the right ventricle was definitely discernible in only a few areas, most of the wall being formed by the thickened endocardium. The trabeculae carneae of the left ventricle were moderately flattened. The pulmonary conus of the right ventricle was particularly dilated. It formed a dome-shaped aneurysm (fig. 4) and contained a reddish-grey, firmly adherent mural thrombus in size rather

FIG. 3.—Interior of right ventricle showing endocardial thickening and parietal thrombus in aneurysm of pulmonary conus.

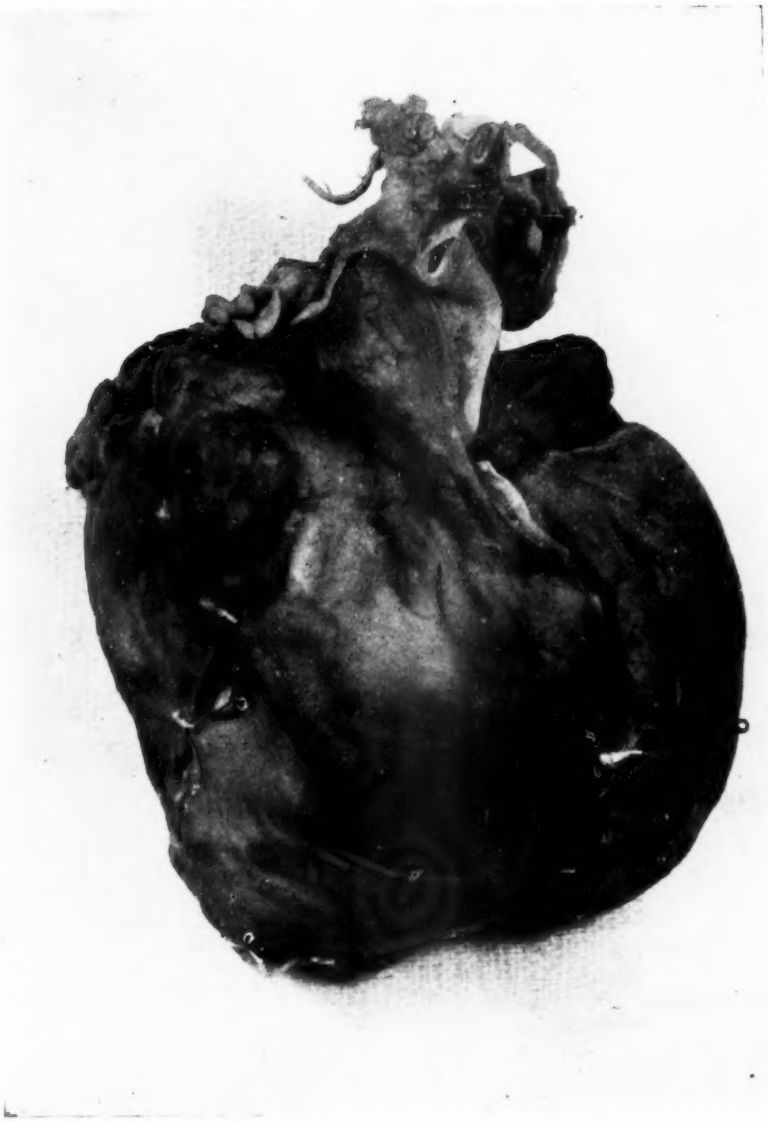

FIG. 4.—Left oblique view of the heart showing the dilated right ventricle and the aneurysm of the pulmonary conus.

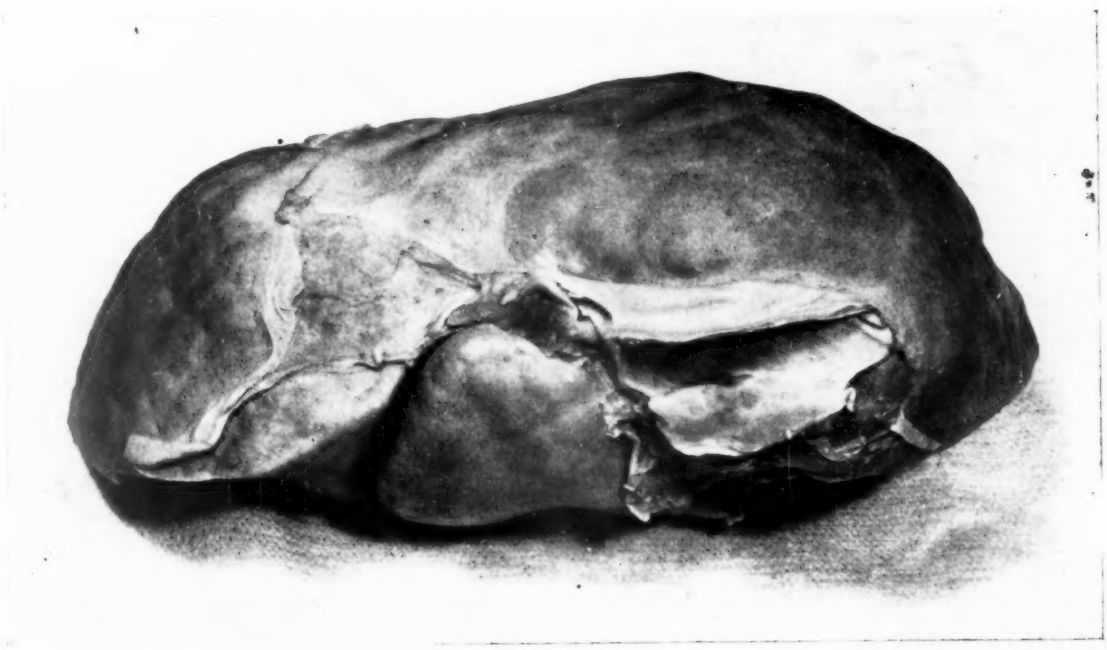

FIG. 5.—Liver.

larger than a walnut (fig. 3). The valves and septa of the heart were normal.

There were approximately three pints of clear straw-coloured fluid in the abdominal cavity. The parietal and visceral peritoneum were normal. The liver was enlarged, weighing 18 oz. The surface was nodular (fig. 5), the colour a pale sandy yellow. The consistency varied, in some parts being very soft, in others harder than normal. On section small red areas were seen with tiny yellow spots without discernible lobular structure and much larger areas yellow in colour with a distinct lobular structure. The spleen was enlarged and fairly hard, weighing 105 g. On section the trabecular pattern was somewhat increased. The kidneys were soft and pale. The ureters and urinary bladder were normal.

The large intestine contained semi-liquid yellow faeces. The mucous membrane was oedematous and hyperaemic. The small bowel and stomach were normal. The mesenteric lymph nodes were normal.

The gall bladder contained green bile; the bile ducts were patent. The pancreas and adrenals were normal.

The skull and dura mater were normal. There was a considerably increased amount of clear fluid in the subarachnoïd space. In a few places the leptomeninges over the vertex had a somewhat milky appearance. The brain was oedematous. The venous sinuses were normal.

The spine and spinal cord appeared normal to the naked eye.

The costo-chondral junctions and the femur were normal. The bone marrow of the latter was red throughout.

ANATOMICAL DIAGNOSIS. Subacute toxic hepatitis. Chronic myocardial degeneration with severe atrophy of the muscle of the right ventricle. Fibroelastosis of the endocardium. Aneurysmal dilatation of the pulmonary conus with mural thrombus. Ascites, Hydrothorax, Anasarca. Oedema of brain and leptomeninges. Acute pericarditis.

BACTERIOLOGY. Direct smears from the pericardium showed numerous polymorphonuclear leucocytes and a few Gram negative bacilli. In cultures K. Friedländer and pneumococci were grown. From the intestine only lactose fermenting organisms were cultured.

Histological findings. LUNG. In several bronchi there was an amorphous eosinophil material containing polymorphonuclear leucocytes and a few red blood corpuscles. There was a moderate cellular infiltration of bronchial walls and peribronchial tissue. The capillaries of the interalveolar septa were dilated and engorged, the alveoli were empty.

TONSIL. No inflammatory changes.

HEART. Sections from right auricle, right ventricle, pulmonary conus, left auricle, left ventricle and interventricular septum were examined. The subendocardial connective tissue, especially that of the right ventricle, was very considerably increased in amount, and consisted of faintly eosinophil, ill-demarcated fibres, with thin fusiform nuclei, surrounding vacuolar spaces and thus causing a resemblance to a honeycomb (fig. 6). Many elastic fibres were seen in this layer in sections stained by the Weigert method (fig. 7). Occasionally a blood vessel with a wall showing hyaline degeneration was seen within the thickened subendocardial tissue. The muscle fibres were extremely atrophic, the majority 5 to 10 μ in diameter, their transverse striation very indistinct or not discernible at all (figs. 8 and 9). Many fibres had a spiral shape. The longitudinal fibrils showed a variety of changes. In some muscle fibres they were well developed throughout the cross section, in others fibrils were seen only in the periphery, the central part being either pale granular or completely colourless like an empty space. Some fibres resembled entirely empty tubes and showed various degrees of spiral coiling. Here and there fibres were seen with transverse or oblique colourless lines. Such lines were often close together within a single muscle fibre and were independent of the 'Kitt Linien.'

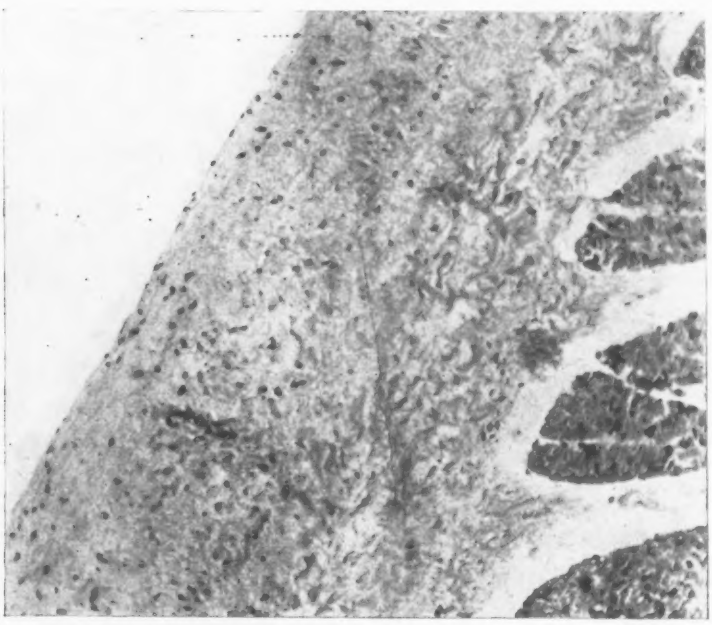

FIG. 6.—Thickened endocardium of right auricle. Haematoxylin and eosin. × 150.

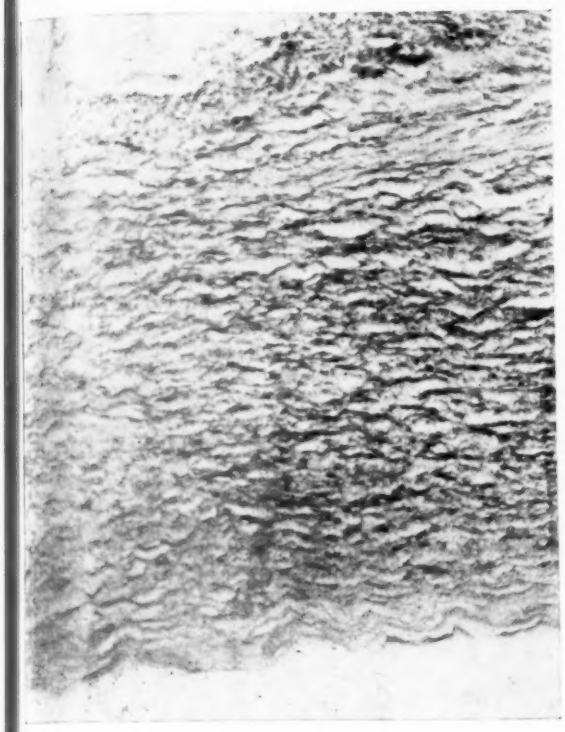

FIG. 7.—Thickened endocardium of pulmonary conus. Weigert's elastic tissue stain. × 150.

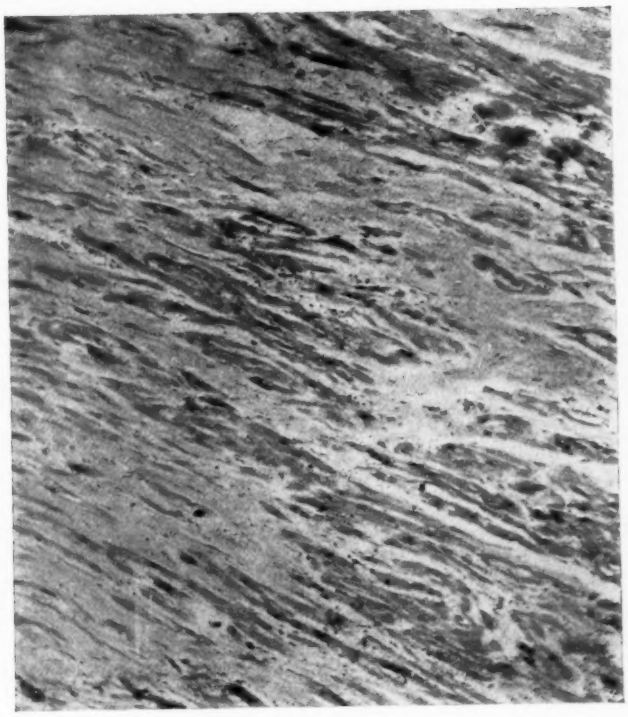

FIG. 8.—Interventricular septum. Haematoxylin and eosin. × 85.

FIG. 9.—Interventricular septum. Haematoxylin and eosin. × 380.

FIG. 10.—Left ventricle. Haematoxylin and eosin. × 670.

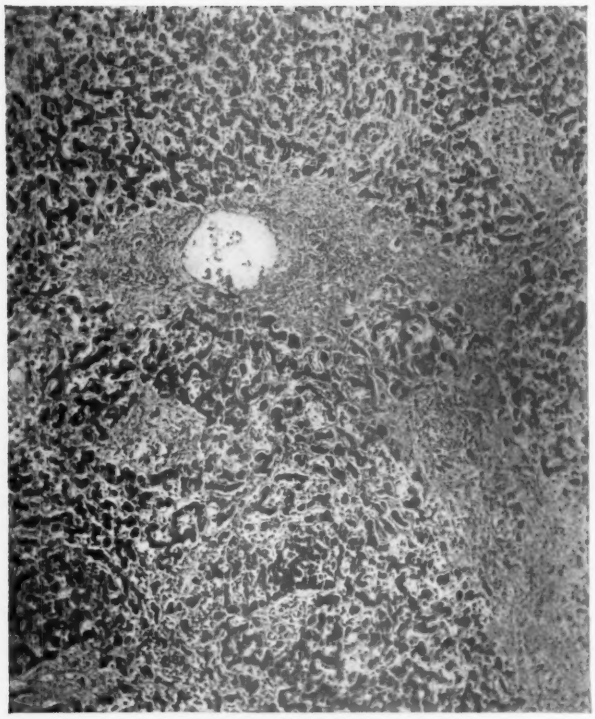

FIG. 11.—Liver. Haematoxylin and eosin. × 85.

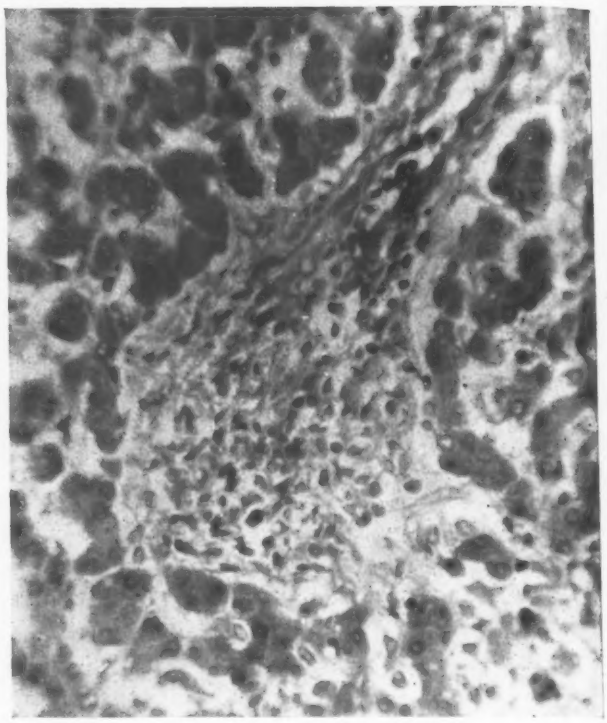

FIG. 12.—Liver showing periportal space with cellular infiltration. Haematoxylin and eosin. × 380.

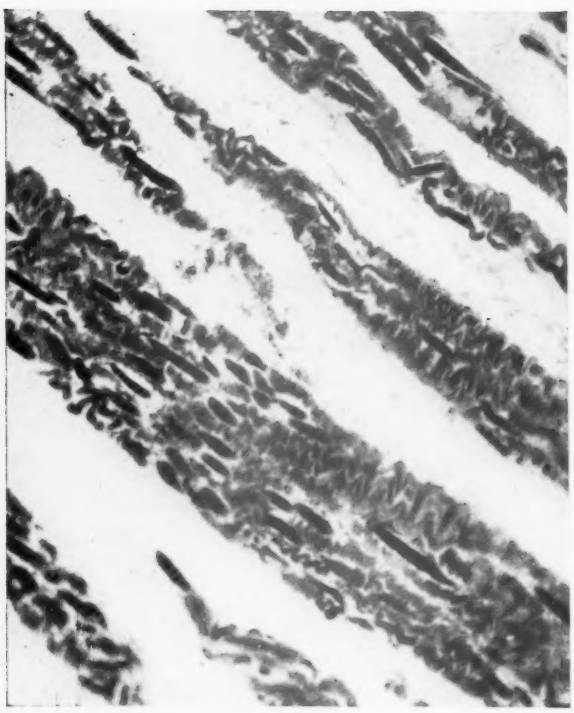

FIG. 13.—M. Quadriceps femoris. Haematoxylin and eosin. × 85.

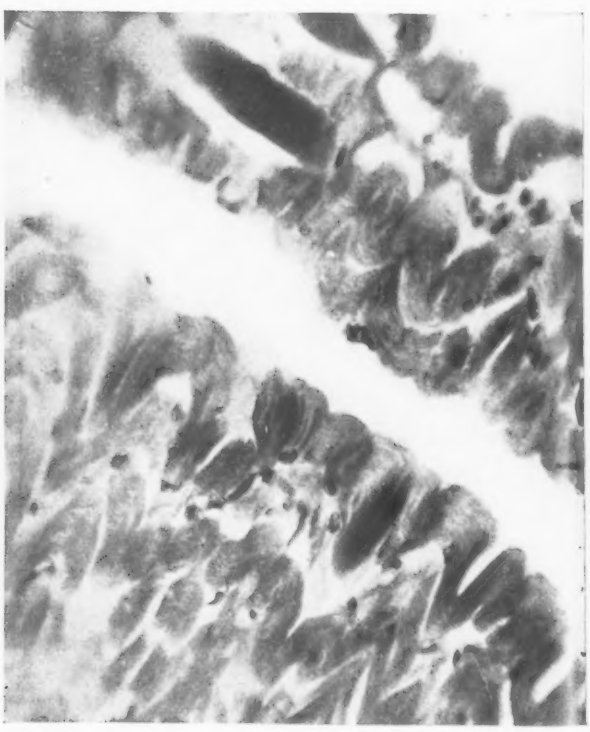

FIG. 14.—M. Quadriceps femoris. Haematoxylin and eosin. × 380.

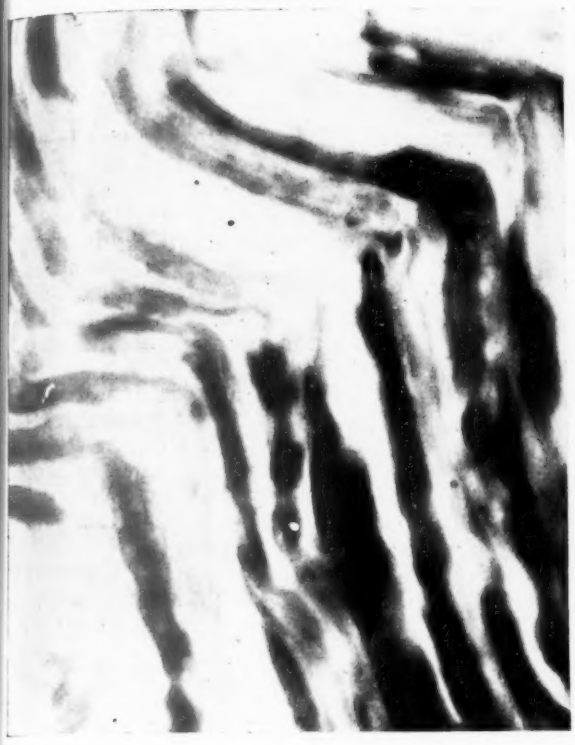

FIG. 15.—Femoral nerve. Weigert-Pal. × 670.

FIG. 16.—Spinal cord, posterior column. Weigert-Pal. × 85.

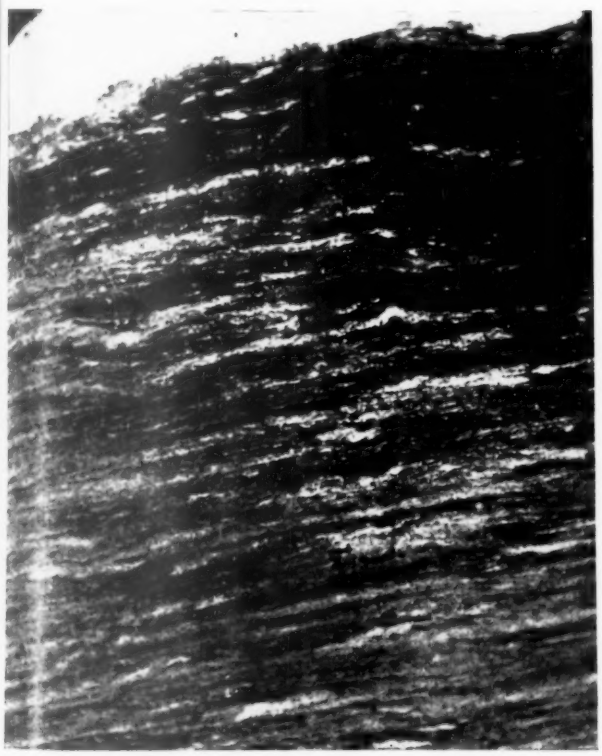

FIG. 17.—Spinal cord, longitudinal section. Weigert-Pal. × 85.

FIG. 18.—Spinal cord, longitudinal section showing balloon-like swelling of myelin sheaths. Weigert-Pal. × 670.

The nuclei had irregular outlines and many showed large spherical colourless areas. Where such changes were most marked the whole nucleus had a foamy appearance with 'vacuoles' separated by thin strands of basichromatin. In some fibres the nuclei filled the whole transverse diameter and the fibres were bulging at this site, showing that the fibre had previously been thicker. In several places the fibres appeared fragmented or merged gradually into a shapeless, granular eosinophil mass in which tiny fusiform nuclei were seen. This hydropic degeneration was especially marked in the subendocardial fibres, while the atrophy was less marked in this region (fig. 10). The subepicardial areolar tissue was oedematous and showed in some areas a diffuse, in others a more circumscribed, infiltration with small round cells.

LIVER. The structure of the liver was completely distorted. No normal lobuli with radially arranged cell trabeculae and a central vein were seen. Instead patches and strands of irregularly arranged liver cells were observed separated by a network of broad strands of connective tissue (fig. 11). The pseudolobuli were in most places smaller than normal lobuli, their shape showed a great variation and in the majority no central vein was visible while in a few an eccentric intralobular vein was present. In some places there was no formation of pseudolobuli; only small groups of liver cells or even single liver cells were seen within a young granulation tissue of periportal origin. The liver cells within the pseudolobuli showed some atrophy due to a dilatation of the capillaries and a moderate number of vacuoles in their cytoplasm. The isolated groups of liver cells showed severe degenerative changes. The Kupffer cells appeared normal. The periportal tissue was considerably increased in amount and formed in sections broad ramifying strands and islands. Its appearance was variable; in some parts it consisted mainly of fibroblasts and collagenous fibres, in other parts there was a marked infiltration with small round cells (fig. 12). The appearance of the bile ducts was normal and there was only a very moderate bile duct proliferation. The arteries and veins were normal. Sections stained by the trichrome method showed a well-preserved network of reticulum fibres. Frozen sections stained by the Herxheimer method showed numerous fat droplets in the liver cells.

KIDNEY. The glomeruli were normal. The epithelium of the first convoluted tubules was swollen, granular and, here and there, a granular eosinophil material was seen in their lumen. The veins of the medulla were distended and engorged.

SPLEEN. The Malpighian bodies were small and consisted almost entirely of germinal centres surrounded by a narrow ring of mature lymphocytes. Here and there were tiny deposits of extravascular hyaline material within the follicles. The venous sinuses were distended and engorged. Red blood corpuscles were also seen within the cords of Billroth. The trabecular tissue was rather conspicuous, the blood vessels were normal.

PANCREAS. Structure normal. The secretory cells contained numerous zymogen granules.

THYROID, ADRENAL, PITUITARY, and THYMUS were all normal.

SKIN. The epidermis was stretched, the stratum papillare partly obliterated and the cutis vera oedematous.

SKELETAL MUSCLE. (M. Quadriceps femoris.) The muscle fibres were atrophic, 7·5 to 25 μ in diameter, the majority being 15 μ. Some of the fibres showed a faint eosin staining, many an indistinct transverse striation and several had a wave-like spiral appearance identical with that described by Meyenburg (1929) in a case of amyotonia congenita (figs. 13 and 14). A similar but less marked change has been depicted by Dürck (1908) in beriberi.

BONE MARROW showed almost pure fatty marrow with small islands of haematopoietic cells. In some areas there were groups of large round cells with cytoplasm containing fine eosinophil granules and an eccentric dark nucleus. These cells were apparently embryonic fat cells.

PERIPHERAL NERVE. (Branch of Femoral Nerve.) The nerve fibres showed areas of complete demyelinization alternating with areas of grossly or moderately swollen myelin sheaths and areas of circumscribed balloon-like swellings (fig. 15).

SPINAL CORD. There were extensive areas of demyelinization mainly in the posterior column (fig. 16), less severe in the lateral tracts and only slightly in the anterior tracts. This demyelinization was patchy in distribution, different sections from the same part of the cord showing a considerable variation in the degree of change. This patchy distribution was best seen in longitudinal sections of the cord, where the alternation of demyelinized and non-demyelinized areas was well shown (fig. 17). The latter sections showed also the balloon-like swellings of the myelin sheaths comparable to those in the peripheral nerve (fig. 18). The axis cylinders showed in Bielschowsky stains moderate changes in the form of tortuosity and fusiform swellings. The degeneration of axis cylinders was well shown in sections stained by Alzheimer's modification of Mann's eosin-methylene blue stain, where many axis cylinders, especially in the posterior tracts, were stained pinkish-red. In several places single fibres or groups of fibres with pink staining axis cylinders were seen among others with a dark purple stain. In the anterior horns of the spinal cord, cells were seen with disappearance of Nissl's granules and with pale or unrecognizable nuclei. The intracellular neurofibrils were preserved in some cells, disintegrated into fine granular material in others.

BRAIN. The nerve cells of the cerebral cortex showed only a moderate degree of chromatolysis. In the inferior olive there were several cells showing a spherical swelling of the cytoplasm and a dark nucleus shifted to the periphery, corresponding to Nissl's 'primary irritation.' Other cells showed a very pale or scarcely recognizable nucleus.

Discussion

The gross anatomical and histological findings justified the diagnosis of beriberi for the following reasons:—

There was a combination of a severe cardiac disease without valvular involvement with degenerative changes in the nervous system.

The cardiac changes, although unusual in some respects, were exactly what one would expect to find if the acute beriberi heart or 'Shoshin,' as described by Wenckebach (1934), were to run a subacute course.

The findings in the nervous system conformed well

with those described in typical cases of beriberi and in experimental vitamin B_1 deficiency.

To consider the cardiac changes: according to Wenckebach the characteristic findings in the acute beriberi heart were an enlargement of the whole heart, but much more of the right side than of the left, a striking dilatation and elongation of the pulmonary conus and a hydropic degeneration of the muscle fibres causing a pseudo-hypertrophy. Wenckebach claimed that the enlargement of the right heart was due to a distension by stagnating blood and the thickening of the wall to a hydropic degeneration rather than to a true hypertrophy. This claim has been challenged by other authors, especially Weiss and Wilkins (1936). Our case does not afford a basis for taking part in this discussion. The main gross anatomical findings, the principal involvement of the right heart and the dilatation of the pulmonary conus were in agreement with Wenckebach's description of a typical beriberi heart. Most of the histological findings, like vacuolar degeneration, shifting (real or apparent) of the fibrils towards the periphery, forming of empty tubes, etcetera, were identical with those which Wenckebach described and supported by photographs. The degenerative atrophy of the muscle fibres, which resulted in the wall of the right ventricle being thinner than normal instead of thicker, may have developed after a previous real hypertrophy or, more likely, after a pseudohypertrophy due to hydropic swelling. This again conformed with the comparatively long duration of the illness.

Dürck (1908), in his classical monograph on the morbid anatomy of beriberi, described cases, some with hypertrophy of the heart, others with an atrophy of the heart muscle, and an occasional case in which there was evidence that an atrophy developed secondary to a primary hypertrophy.

The pericarditis was a recent one, obviously a terminal complication. There was no evidence of acute or chronic endocarditis or myocarditis. The valves were normal. No congenital anomaly was detected.

The unusual findings in our case, the aneurysmal dilatation of the conus with the formation of a parietal thrombus and the fibro-elastosis of the endocardium were easily explained by the fact that Wenckebach's patients were acute whereas ours ran a subacute course. The changes in the pulmonary conus were only an exaggeration of those described by Wenckebach, while the fibro-elastosis represented the reaction of the heart to prolonged passive distension and was occasionally observed in lesser degree by Dürck.

Mural thrombi in the auricles were described by Ashburn and Lowry (1944) in experimental thiamin deficiency. In man a syndrome of cardiac hypertrophy, dilatation with the presence of mural thrombi, has been described by a number of observers. Dock (1940) reported five fatal cases, in three of which the diagnosis of beriberi was deemed to be established and considered to be possible in the other two. Smith and Furth (1943) recorded five similar cases and reviewed the literature. The essential pathological features were an endocardial and myocardial fibrosis with cardiac hypertrophy and dilatation in the absence of vascular or valvular damage. Considering its etiology they were of the opinion that the causation was a nutritional deficiency, but were unable to say that vitamin B was the factor responsible. On the other hand, Levy and von Glahn (1944), who described ten fatal cases of uncomplicated cardiac hypertrophy, dilatation with mural thrombi in the ventricles, found no evidence that a vitamin deficiency contributed to the cause. Although the histological changes were not identical there was a definite similarity between the three series of cases, which lends support to the observation of Weiss and Wilkins (1936), that hydropic degeneration of cardiac muscle fibres is not absolutely specific for beriberi. Only the totality of the anatomical and histological findings in the heart and in the nervous system can justify the diagnosis of beriberi in a sporadic case.

The changes in the nervous system in beriberi have been more extensively studied than those in the myocardium. Several authors have compared the neurohistology of beriberi with pellagra. Although there is still some controversy as to whether the neurohistology of beriberi is specific for this disease and due to a thiamin deficiency or is a result of starvation (Spillane, 1945), there is close agreement with regard to the principal microscopical findings in the nervous system of beriberi cases. Dürck (1908), Rodenwaldt (1908), Winkelman (1926), Cannon (1929–30), Shimazono (1931), Langworthy (1931), Zimmerman and Cowgill (1937), Zimmerman (1939–40) and Hsü Ying-K'Uei (1942) all describe myelin degeneration, demyelinization, degeneration of axis cylinders in the peripheral nerves and in the fasciculi of the spinal cord. The involvement is described as progressing from the periphery towards the centre, the sensory fibres are more involved than the motor and the thick fibres more than the thin. In the spinal cord Rodenwaldt stressed the degeneration of the column of Burdach. A patchy distribution of the degeneration appears to be rather characteristic. Dürck states that the myelin degeneration within the continuity of a single fibre is always spotty and segmentary and that one fibre may be quite intact over part of its length while in various other parts advanced disintegration, fatty metamorphosis and resorption of the myelin may be observed. The findings in our case are, so far as nerve fibres are concerned, of the same nature as those described in authentic cases from endemic areas. There is less conformity in the literature with regard to the nerve cells than to the nerve fibres. Nissl's ' primary irritation,' observed in a few places in our case, belongs according to Zimmerman and to Hsü Ying-K'Uei to the pellagra and not to the beriberi syndrome. The hyalinization of the walls of blood vessels and the ' diffuse parenchymal fatty degeneration ' observed by Winkelman in pellagra were not

seen in our case. The primary irritation is characteristic of retrograde degeneration (Spielmeyer, 1922) and it is not surprising to meet this change in beriberi.

The severity of the degenerative changes in the skeletal muscle of our case is remarkable.

An unusual finding was the cirrhosis of the liver. Typical cases of beriberi with cirrhosis of the liver have not been described to our knowledge, nor was liver cirrhosis produced experimentally by thiamin deficiency. The problem of nutritional cirrhosis of the liver has been thoroughly studied in recent years by György and Goldblatt (1939), Lillie, Daft and Sebrell (1941), Himsworth and Glynn (1944) and others. The existence of a liver cirrhosis due to a nutritional deficiency can be considered as well established. It is not known whether a specific vitamin can be made responsible for cirrhosis of the liver and it is certain that other factors like the relation of fat to protein in the diet play an important rôle in the development of nutritional liver disease. It is, therefore, not justified to consider the changes in the liver as due to the same cause as those in the myocardium and in the nervous system. They are rather to be attributed to another associated dietary deficiency.

As the liver disease was of long standing it is possible that it contributed to the development of a vitamin B deficiency state. In cases of liver damage there is a high urinary excretion of thiamin following a series of oral loading doses, amounting in some cases to 50 per cent. of the dose given, normal figures being about 20 per cent. (Allibone and Finch, 1945). In our patient there was no question of a dietary thiamin deficiency. When first seen his diet contained at least 0·75 mg. thiamin a day, which rose after his first admission to 0·9 mg. a day, exclusive of medication which was intermittent. Knott (1936) considered an intake of 60 microgm. per kilo body weight to be optimal. On this basis the optimal daily thiamin intake for our patient, who weighed 30 lb., would have been 0·8 mg. The adequacy of the diet, together with the rarity of beriberi in England, indicates the severity of the metabolic dysfunction which led to the deficiency.

At the time of the boy's first admission the low plasma protein and the hypocalcaemia suggested a nutritional deficiency state. Although the blood pyruvic acid level was definitely raised beriberi was not further considered. On readmission the overshadowing syndrome of congestive heart failure in a child of three and a half years without evidence of valvular heart disease and who previously had had symptoms of nutritional deficiency, cause investigations and treatment to be concentrated on the beriberi aspect of the clinical picture. The cases of myocardial fibrosis described by Dock (1940), Smith and Furth (1943) and Levy and von Glahn (1944) were all fatal. A characteristic of these patients was the failure to respond to vitamin therapy and although remissions might occur, these seemed to be spontaneous. Although the fall of the blood pyruvic acid level with vitamin B therapy in our boy was as rapid as could be expected, he too went rapidly downhill. The morbid histology of the heart seems to explain adequately the course of such cases.

Wenckebach (1934) commented on the surprising rapidity with which symptoms of acute beriberi heart (Shoshin) develop and the equal rapidity with which they may be alleviated. It is nevertheless remarkable that a boy with such chronic and irreversible cardiac damage could have been active and running about until eight days before he died.

The typical radiological configuration of right-sided cardiac dilatation, as described by Wenckebach, was partly masked by the 4 to 5 oz. of fluid in the pericardium.

There is no unanimity as to the form of the electrocardiogram in beriberi. Wenckebach (1934) in Java found no essential change, nor did Keefer (1930) in China. Neither Jones and Bramwell (1939) nor Konstam and Sinclair (1940) saw anything gross in the electrocardiogram of their cases. In experimental thiamin deficiency Williams et al. (1940) observed flattening of the T wave which became larger when vitamin was added to the diet. Weiss and Wilkins (1936) found changes in the T wave, a prolonged Q–T and a low voltage QRS in over 90 per cent. of their cases. Goodhart and Jolliffe (1938) noted depression of the S–T segments and inverted T waves in their cases. Dock (1940) recorded alteration of the ventricular complex suggestive of a myocardial infarct. It seems likely that the abnormalities are proportional to the degree of chronic or permanent damage.

The very large P wave in our patient, particularly when compared with the absent T wave suggested a hypertrophy of the auricles, a condition which may occur when they are subject to undue stress by a failing ventricle. Why the auricle should be capable of undergoing hypertrophy while the ventricular muscle degenerates is unknown. An accentuated P wave was observed by Smith and Furth (1943) in one of their fatal cases of chronic myocarditis attributed to nutritional deficiency.

Summary

A fatal case of beriberi is described. The relationship of the myocardial changes to those found in acute beriberi and in myocardial fibrosis is discussed.

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REFERENCES

Allibone, E. C., and Finch, E. (1945). *Arch. Dis. Childh.*, **20**, 169.
Ashburn, L. L., and Lowry, J. V. (1944). *Arch. Pathol.*, **37**, 27.
Bates, J. (1941). *Lancet*, **1**, 176.
Cannon, A. (1929–30). *Trans. Roy. Soc. Trop. Med. Hyg.*, **23**, 263.
Dock, W. (1940). *Trans. Ass. Amer. Physicians*, **55**, 61.
Dürck, H. (1908). Untersuchungen über die pathologische Anatomie der Beriberi. *Suppl. der Beiträge zur pathologischen Anatomie*, Jena.

Ellis, R. W. B. (1945). *Arch. Dis. Childh.*, **20,** 97.
Goodhart, R., and Jolliffe, N. (1938). *Amer. Heart J.*, 15, 569.
György, P., and Goldblatt, H. (1939). *J. exper. Med.*, 70, 185.
Himsworth, H. P., and Glynn, L. E. (1944). *Lancet*, **1,** 457.
Hsü Ying-K'Uei (1942). *Arch. Neurol. Psychiat.*, Chicago, **48,** 271.
Jones, A. M., and Bramwell, C. (1939). *Brit. Heart J.*, **1,** 187.
Keefer, C. S. (1930). *Arch. intern. Med.*, **45,** 1.
Knott, E. M. (1936). *J. Nutrit.*, **12,** 597.
Konstam, G., and Sinclair, H. M. (1940). *Brit. Heart J.*, 2, 231.
Langworthy, O. R. (1931). *Brain*, **54,** 291.
Levy, L., and von Glahn, W. C. (1944). *Amer. Heart J.*, **28,** 714.
Lillie, R. D., Daft, F. S., and Sebrell, W. H. (1941). *Publ. Hlth. Rep.*, Washington, **56/1,** 1255.
Meyenburg, H. von. (1929) in Henke and Lubarsch: *Handb. path. Anat. u. Histol.*, **9,** Part 1, Berlin.
Pyke, M. (1945). *Brit. med. J.*, **2,** 839.
Rodenwaldt, E. (1908). *Arch. Schiffs-u Tropen Hyg.*, **12,** 31.
Shimazono, J. (1931). *Erg. inn. Med. Kinderh.*, **39,** 1.
Smith, J. J., and Furth, J. (1943). *Arch. intern. Med.*, **71,** 602.
Spielmeyer, W. (1922). *Histopathologie des Nervensystems*, Berlin.
Spillane, J. W. (1945). *Lancet*, **2,** 449.
Weiss, S., and Wilkins, R. W. (1936). *Trans. Ass. Amer. Physicians*, **51,** 341.
Wenckebach, K. F. (1934). *Das Beriberi-Herz*, Berlin.
Williams, R. D., Mason, H. C., Wilder, R. M., and Smith, B. J. (1940). *Arch. intern. Med.*, **66,** 4.
Winkelman, N. W. (1926). *Zeit. ges. Neurol. Psychiat.*, **102,** 38.
Zimmerman, H. M. (1939). *Yale J. Biol. Med.*, **12,** 23.
—— and Cowgill, G. R. (1937). *Arch. Neurol. Psychiat.*, **37,** 286.

PENICILLIN AND SULPHONAMIDES IN THE TREATMENT OF INFECTIONS IN INFANCY

BY

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In a previously reported series of cases, treatment with penicillin alone gave encouraging results and it was decided to test the efficacy of combining penicillin and sulphonamide therapy. The previous cases were treated during the months of September, October and November and the series about to be described was treated during the first six months of the year. This is a matter of some importance in planning the experiment and in assessing the results, since the virulence of the infections to which infants are prone seems to be greatest in the early months of the year.

There are now many sulphonamide drugs from which to choose but they may be divided broadly into two groups: (a) the well-absorbed sulphonamides which may be described as anti-coccal in action, e.g. sulphathiazole and sulphadiazine, and (b) the poorly absorbed sulphonamides which may be described as anti-bacillary in action, e.g. sulphasuxidine and sulphaguanidine. Sulphathiazole has been selected as representative of the first group and sulphasuxidine of the second. Bacteriological investigations show that infections by organisms of the colon bacillus group are common in the early months of life and it is possible that the use of a drug such as sulphasuxidine, which reduces the number of B. Coli in the intestinal tract, may be of benefit. Glucose-saline by mouth was administered both to overcome dehydration if present and to assist in the elimination of the sulphonamide in the cases so treated. Subcutaneous salines and intravenous salines were also given as required.

Part I

From the above considerations it was decided to treat three sets of cases concurrently as follows:—

(A) A group treated with penicillin alone, in order to confirm that the good results previously obtained in September, October and November were continued in January, February and March.

(B) A group treated with penicillin and sulphathiazole to test the efficacy of penicillin plus a well-absorbed, anti-coccal sulphonamide which might reinforce the action of penicillin against penicillin and sulphonamide sensitive cocci.

(C) A group treated with penicillin and sulphasuxidine to test the efficacy of penicillin plus a poorly absorbed, anti-bacillary sulphonamide which might reduce the numbers of B. Coli in the intestinal tract and minimize infection or prevent terminal invasion by these organisms.

Type of case. The type of case treated was as follows: bronchopneumonia, nasopharyngitis, otitis media and premature infants who go gradually downhill, a type which is frequently found at post-mortem examination to have some infection which has eluded detection in life.

Dosage. Penicillin was made up in bottles containing 25,000 units dissolved in 8 c.c. of saline, and was given in 1 c.c. doses intramuscularly at three-hourly intervals. each bottle lasting twenty-four hours. Occasionally twice this amount of penicillin was used.

Sulphonamide. An initial dose of 0·5 to 0·75 g. was given followed by 0·25 g. three-hourly. This smaller dose was given in order to coincide with the injections of penicillin. The usual dose for a mature infant in this hospital is 0·5 g. four-hourly.

Glossary of Abbreviations.

D = Diarrhoea. W = Weight loss.
V = Vomiting. T = Pyrexia.
De = Dehydration. N.W. = Not weighed.
Cy. = Cyanosis.

Group A: Penicillin alone

Of this group eight were considered to be severely ill, three moderately ill and one mildly ill. The eight severely ill cases died. The high incidence of prematurity in this group will be noticed. This is due to the tendency, difficult to avoid, to give penicillin alone to premature infants so that their normal feeds may be continued as far as possible. The use of sulphonamides necessitates substituting glucose saline to assist the elimination of the drugs.

SYMPTOMS. In addition to the symptoms of the disease from which they suffered, these infants showed the following general symptoms: diarrhoea 5, vomiting 3, dehydration 8, pyrexia 2, loss of weight 9 and 3 were too ill to be weighed. In the case with pyaemia the temperature was uncontrolled. Loss of weight varied from 5 to 16 oz.

COURSE OF THE ILLNESS. Among those who died, five improved at first and then relapsed. Another was doing well when its parents insisted on removing the infant from hospital against advice and brought

TABLE I

GROUP A: PENICILLIN ALONE

Case No.	Diagnosis	Clinical grade	General signs	Penicillin units	Alive	Dead
1	Prematurity, bronchopneumonia and pemphigus	Severe	D, T, W	193,750		D
2	Prematurity, bronchopneumonia	Severe	D, De, W	21,875		D
3	Prematurity, bronchopneumonia and nasopharyngitis.	Severe	D, De, W	450,000 300,000		D
4	Prematurity, jaundice, bronchopneumonia, bilateral acute otitis media.	Severe	De, NW	365,000		D
5	Prematurity, jaundice, bronchitis and right acute otitis media.	Severe	De, W	225,000 100,000		D
6	Prematurity, jaundice, bronchopneumonia and nasopharyngitis.	Severe	De, NW	225,000		D
7	Prematurity, right acute otitis media with profuse otorrhoea.	Mild	V, W	350,000 Pen. drops locally	A	
8	Prematurity, jaundice, sclerema, atelectasis, haemorrhages into lungs, left otitis media and mastoiditis.	Severe	NW	15,615		D
9	Prematurity; condition deteriorating	Moderate	De, W	200,000	A	
10	Prematurity, jaundice, pyaemia, left otitis media ..	Severe	D, V, De, W, T	425,000 125,000		D
11	Prematurity, jaundice; condition deteriorating ..	Moderate	De, W	350,000 300,000	A	
12	Bilateral acute otitis media	Moderate	D, V, W	75,000	A	
					4	8

her back a few days later moribund. The infant (case No. 10) who had pyaemia did very well with the first course of penicillin and its weight rose from 3 lb. 12 oz. to 5 lb. when an abscess and cellulitis developed on the buttock some weeks after penicillin had been stopped. Two required subcutaneous salines and in one case the buttocks broke down. In case No. 11 improvement coincided with doses of penicillin of 50,000 units per day instead of the usual 25,000 units, but in case No. 1 the larger doses were of no avail. The otorrhoea in case No. 7 continued for fourteen days but ceased in three days with penicillin drops (1000 units per c.c.) locally, and the acute inflammation of the tympanic membranes in case No. 12 settled quickly in three days. In those who recovered, weight, lost as a result of the illness, was regained in nine to twenty-three days.

BACTERIOLOGY IN LIFE. Faeces were examined in all the cases but no pathogenic organisms were discovered. In case No. 3, a severe nasopharyngitis with much nasal discharge, the nasal swab grew Staphylococcus aureus, sensitive to penicillin and sulphonamides. A second nasal swab, thirteen days later, grew coliform organisms, resistant to penicillin but sensitive to sulphonamide, and Staphylococcus albus, sensitive to penicillin and resistant to sulphonamide. Case No. 7 had profuse otorrhoea and swab from the discharge grew coliform organisms resistant to penicillin and sulphonamide. In spite of this, response to penicillin therapy was good and discharge ceased three days after local application of penicillin drops. Pus from the buttock abscess in case No. 10 grew Staphylococcus aureus, sensitive to penicillin but resistant to sulphonamide.

POST-MORTEM FINDINGS. Permission for post-mortem examination was obtained in the eight cases who died. In cases Nos. 1, 2, 3 and 4 the presence of bronchopneumonia was confirmed by microscopic sections of the lungs. Case No. 4 also had bilateral otitis media. Case No. 5 showed the presence of bronchitis and right otitis media, while in case No. 6 there was bronchopneumonia and haemorrhages into the skin of the buttocks which were thought to be due to the injections. The lungs in case No. 8 showed complete atelectasis of the left lower lobe with extensive haemorrhages into the fully expanded parts of the lungs and blood in the trachea. From this point of view this was not a suitable case for penicillin therapy but in addition left otitis media and mastoiditis were found. In case No. 10, the case of pyaemia, the spleen was enlarged and septic, and septic infarcts in the lungs and kidneys and left otitis media were found.

POST-MORTEM BACTERIOLOGY. Swabs were taken from the ears in cases No. 4, 5, 8 and 10, with the following results. Direct smears showed coliform organisms and Gram positive cocci in cases No. 4, 5 and 8, coliform organisms alone in case No. 10. Cultures in case No. 4 grew coliform organisms, resistant to penicillin and sensitive to sulphonamide and Staphylococcus albus, sensitive to penicillin and resistant to sulphonamide; in case No. 5 coliform organisms, resistant to penicillin and sensitive to sulphonamide and non-haemolytic streptococci, sensitive to penicillin and resistant to sulphonamide. Culture in case No. 8 was overgrown with coliform organisms, resistant to penicillin and sensitive to sulphonamide, and a similar result was obtained in case No. 10. Swabs were taken from the lungs in cases No. 4 and 5 and results similar to those of the ear swabs were obtained.

TABLE 2

GROUP B: PENICILLIN AND SULPHATHIAZOLE

Case No.	Diagnosis	Clinical grade	General signs	Penicillin (units)	Thiazole g.	Alive	Dead
1	Bronchopneumonia, otitis media and mastoiditis.	Severe	D, De, W	381,250	4·5		D
2	Prematurity, bronchopneumonia and nasopharyngitis	Severe	D, V, De, W	150,000	5·0		D
				50,000	2·5		
3	Bilateral otitis media	Severe	D, V, De, T, W	100,000	4·75	A	
				100,000	6·75		
				275,000	6·75		
				225,000	4·75		
				175,000	—		
				425,000	—		
4	Pneumonia and sub-mental abscess	Severe	W	100,000	8·75		D
5	Bilateral otitis media and nasopharyngitis	Moderate	D, W	275,000	5·25	A	
6	Prematurity, nasopharyngitis, bilateral otitis media, bronchopneumonia.	Severe	De, W	65,625	4·75		D
7	Prematurity; condition deteriorating	Moderate	D, V, De, T, W	200,000	6·25	A	
				150,000	2·5		
8	Bilateral otitis media	Moderate	D, W	200,000	6·25	A	
9	Prematurity; condition deteriorating	Mild	De, W	250,000	6·25	A	
10	Bilateral otitis media	Moderate	D, T, W	100,000	6·25	A	
						6	4

Group B: Penicillin and Sulphathiazole

In this group five were judged to be severely ill, four moderately ill and one mildly ill. Four were premature infants and two of these died.

SYMPTOMS. General symptoms occurred as follows: diarrhoea 7, vomiting 3, dehydration 6, pyrexia 3 and loss of weight 10. Temperature, which only lasted for one day after institution of treatment, varied from 101°F.–104·8°F. Loss of weight varied from 4 to 16 oz.

COURSE OF THE ILLNESS. In two of the cases who died (No. 1 and 2) improvement occurred at first and the patients then relapsed. In the other two no improvement was manifest. Three cases who recovered suffered from otitis media, No. 5, 8 and 10, and the inflammation of the tympanic membranes settled in three days, seven days and eleven days respectively. The remainder progressed satisfactorily except case No. 3, which also suffered from otitis media. In this case relapse took place on five occasions with losses of weight varying from 5 to 16 oz. The tympanic membranes seemed to settle in periods from three to eight days on the first four occasions but in the last two no evidence of parenteral infection could be found. Sulphathiazole was given with the first four courses of penicillin but not with the last two. The response was just as favourable without the sulphathiazole. Figure 1 shows this infant's weight curve from the beginning of its illness till the date of its discharge from hospital and the response to treatment is clearly demonstrated. It may be noted that at the first relapse treatment seems to have begun before weight was lost. This appearance of the graph is due to the fact that the infant became very ill the night before, when treatment was begun, and was not weighed till the following morning. At the third relapse, left myringotomy was performed as the child was very ill and dehydrated. A small bead of pus was released. The constant response to penicillin treatment suggests that this was almost certainly a penicillin-sensitive infection. In those who recovered, weight lost as a result of the illness was regained in periods varying from four to thirteen days.

BACTERIOLOGY IN LIFE. In nine instances bacteriological examination of the faeces showed no evidence of pathogenic organisms. In one case a specimen was not obtained. Case No. 2 had severe nasopharyngitis with copious nasal discharge and on two occasions swabs were taken. In the first Staphylococcus aureus, sensitive both to penicillin and sulphonamide, was grown and in the second Staphylococcus aureus, sensitive to penicillin but resistant to sulphonamide. In case No. 3 myringotomy released a small bead of pus and an attempt was made to culture with negative result. Pus from the submental abscess in case No. 4 grew Staphylococcus aureus, sensitive to penicillin and sulphonamide.

POST-MORTEM FINDINGS. Permission for post-mortem examination was obtained in three of the four fatal cases with the following results. In cases No. 1 and 6 the presence of bronchopneumonia was confirmed by microscopic section. In case No. 3 microscopic section looked more like haemorrhages into the lung and congestion. In case No. 1 left otitis media and mastoiditis were found in addition and left otitis media in case No. 6.

POST-MORTEM BACTERIOLOGY. Swabs from the lungs and mastoid antra in case No. 1, when cultured, grew coliform organisms, resistant to penicillin and sensitive to sulphonamide and streptococcus faecalis, resistant to both penicillin and sulphonamide. Direct smear from the lung in case No. 2 showed Gram positive cocci and cultures grew diphtheroids, sensitive to penicillin but resistant to sulphonamide. Culture from the middle ear in case No. 6 grew coliform organisms, resistant to

TABLE 3

GROUP C: PENICILLIN AND SULPHASUXIDINE

Case No.	Diagnosis	Clinical grade	General signs	Penicillin (units)	Suxidine g.	Alive	Dead
1	Bilateral acute otitis media	Moderate	D, De, T, W	150,000	5·5	A	
2	Bilateral acute otitis media	Mild	W	350,000	4·5	A	
3	Bilateral acute otitis media	Moderate	D, V, De, W	250,000	5·75	A	
4	Bilateral acute otitis media	Severe	D, V, De, W	100,000	6·25	A	
5	Prematurity, jaundice; condition deteriorating..	Moderate	De, W	200,000	6·5	A	
6	Prematurity, bronchopneumonia	Severe	W	175,000	6·5		D
7	Prematurity, ? otitis media	Moderate	D, V, De, W	200,000 255,000	6·0 6·0	A	
8	Bilateral acute otitis media	Severe	D, T, W	150,000	5·75	A	
9	Prematurity, jaundice; condition deteriorating	Severe	D, V, De, W	175,000	6·25	A	
10	Prematurity, bronchopneumonia	Moderate	De, W, Cy	150,000	6·25	A	
11	Bilateral acute otitis media	Moderate	V, De, W	175,000	6·75	A	
12	Bilateral acute otitis media	Severe	D, V, De W	375,000	4·5	A	
13	Prematurity, jaundice; condition deteriorating..	Moderate	De, W	300,000	5·75	A	
14	Bilateral acute otitis media	Mild	D, V, De, W	100,000	10·75	A	
15	Bilateral acute otitis media and nasopharyngitis.	Moderate	V, De, T, W	175,000	6·25	A	
						14	1

penicillin and sensitive to sulphonamide. Direct smear from the right middle ear showed some Gram positive cocci.

Group C: Penicillin and Sulphasuxidine

Five cases in this group were judged to be severely ill, eight moderately ill and two mildly ill. Six were premature infants of whom one died.

SYMPTOMS. General symptoms occurred as follows: diarrhoea 8, vomiting 8, dehydration 12, pyrexia 3 and loss of weight 15. Temperature again only lasted one day after institution of treatment and varied from 99·8°F. to 101°F. Loss of weight varied from 4 to 21 oz.

COURSE OF THE ILLNESS. There were nine cases of otitis media in whom the inflammation of the tympanic membranes settled in from three to eighteen days. In three an unusual phenomenon was observed. The inflammation seemed to come and go. One day the drums looked nearly normal and the next day as acutely inflamed as ever. These cases ultimately settled down completely. One was sufficiently dehydrated to require intravenous fluids; in two others the general response was rather slow, and in another, which also had nasopharyngitis, the ears settled clinically in six days but the nasopharyngitis continued for a longer period. Two of the premature infants required subcutaneous salines but, except for one who required two courses of treatment and in whom feeding difficulty was encountered, their progress was uneventful. Those who recovered regained weight lost as a result of the illness in periods varying from three to sixteen days.

BACTERIOLOGY IN LIFE. In thirteen cases bacteriological examination of the faeces showed no evidence of pathogenic organisms, one being examined on two occasions. In one case faecal streptococci were grown and in another a specimen was not obtained.

POST-MORTEM FINDINGS. Post-mortem examination in the case who died revealed the presence of bronchopneumonia confirmed by microscopic section.

POST-MORTEM BACTERIOLOGY. Direct smear from the lungs showed coliform organisms and culture grew coliform organisms, resistant to penicillin but sensitive to sulphonamide and non-haemolytic streptococci, sensitive to penicillin but resistant to sulphonamide.

Part II

From the results described in Part I it would appear that the best results are obtained from the combination of penicillin and sulphasuxidine. The experiment was continued on these lines and two further groups remain to be described.

(A) A group treated with penicillin and sulphasuxidine to confirm the good results already obtained.

(B) A group treated with sulphasuxidine alone to test the efficacy of this drug in such infections.

Group A

Of this group nine were severely ill, ten moderately ill and one mildly ill. There were ten premature infants, of whom five died.

SYMPTOMS. General symptoms were as follows: diarrhoea 5, vomiting 3, dehydration 9, pyrexia 5

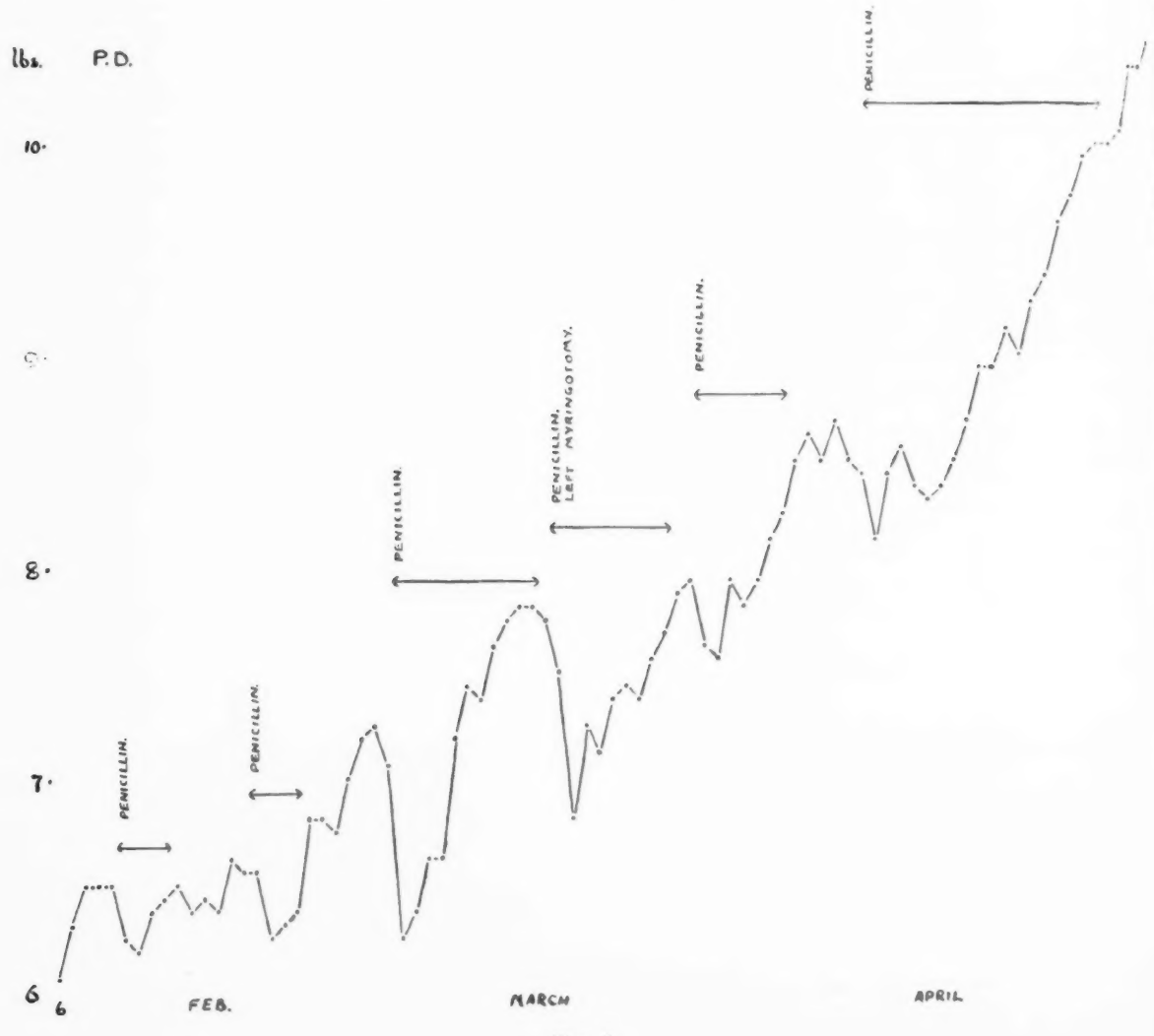


FIG. 1.

and loss of weight 16. Five premature infants had cyanotic attacks. In one case weight was stationary and three were too ill to be weighed. Temperature, which varied from 99°F. to 105·3°F., settled in three cases in one to two days after treatment was begun. In the remaining two, temperature took twelve and twenty-seven days respectively to settle. Weight loss varied from 4 to 20 oz.

COURSE OF THE ILLNESS. Nine cases were diagnosed in life as suffering from otitis media. In these the inflammation of the tympanic membranes settled clinically in from five to twenty-three days. In three the 'coming and going' type of inflammation was noted. In two cases one ear only was affected to begin with, but the treatment did not prevent the other ear from becoming affected subsequently, as in case No. 9, in whom the otorrhoea ceased in six days but the other ear became acutely inflamed later, and took eleven days to settle clinically. The five deaths were premature infants, in all of whom bronchopneumonia was diagnosed. The remaining five premature infants consisted of two cases of bronchopneumonia, one of bronchitis and two were going steadily downhill. The progress of these cases was very satisfactory. In case No. 6 one buttock became rather indurated, but subsided when injections were stopped. Case No. 13 did not progress well and required intravenous fluid. Those who recovered regained weight lost as a result of the illness in periods varying from six to forty-five days.

BACTERIOLOGY IN LIFE. In fifteen cases bacteriological examination of the faeces showed no evidence of pathogenic organisms. One specimen grew B. Morgan I and in four cases specimens were not obtained. A swab of the aural discharge in case No. 9 was taken and direct smear showed Gram positive cocci and coliform organisms. Culture grew Staphylococcus aureus, sensitive to penicillin and sulphonamide, and coliform organisms, resistant to penicillin and sensitive to sulphonamide. Fig. 2 is a photograph of the culture plate in this case. The upper test is the penicillin sensitivity test, where the colonies of resistant coliform organisms can be seen. In case No. 17, which had an abscess of the thigh, direct smear of the pus showed Gram positive cocci, while the culture plate was overgrown with coliform organisms.

TABLE 4

GROUP A: PENICILLIN AND SULPHASUXIDINE

Case No.	Diagnosis	Clinical grade	General signs	Penicillin (units)	Suxidine g.	Alive	Dead
1	Bilateral otitis media, jaundice, congenital heart disease.	Moderate	D, V	475,000	6·5	A	
2	Prematurity, jaundice; condition deteriorating..	Moderate	D De, W.	200,000	6·5	A	
3	Prematurity, jaundice; condition deteriorating..	Moderate	T, W	200,000	6·25	A	
4	Bilateral otitis media	Mild	W	275,000	6·0	A	
5	Prematurity, bronchitis and nasopharyngitis ..	Moderate	De, T, W	325,000	6·25	A	
6	Bilateral otitis media and nasopharyngitis ..	Moderate	T, W	300,000	5·0	A	
7	Bilateral otitis media	Moderate	D, De, W	375,000	6·5	A	
8	Bilateral otitis media	Moderate	D, De, W	400,000	6·5	A	
9	Right otitis media and otorrhoea; left otitis media.	Moderate	T	175,000 275,000	6·5 6·5	A	
10	Prematurity, bronchopneumonia, right otitis media and subdural haemorrhage.	Severe	Cy	75,000	6·5		D
11	Prematurity, jaundice, bronchopneumonia ..	Severe	De, W	75,000	6·5		D
12	Prematurity, bronchitis, bilateral otitis media ..	Severe	W	6,250	0·75		D
13	Bilateral otitis media	Severe	D, V, De, T, W	175,000 150,000 200,000	6·5 — 6·5	A	
14	Bronchitis	Moderate	De, W	200,000	6·5	A	
15	Jaundice, bilateral otitis media	Moderate	W	650,000	6·5	A	
16	Prematurity, bronchopneumonia and nasopharyngitis.	Severe	N, W, Cy	150,000 75,000	6·5 4·5	A	
17	Right otitis media and abscess of thigh	Severe	V, De, W	175,000	6·25	A	
18	Prematurity, bronchopneumonia	Severe	De, W, Cy	100,000	6·5		D
19	Prematurity, bronchopneumonia	Severe	N, W, Cy	9,375	1·0		D
20	Prematurity, bronchopneumonia	Severe	Cy	200,000 250,000	6·5 6·5	A	
						15	5

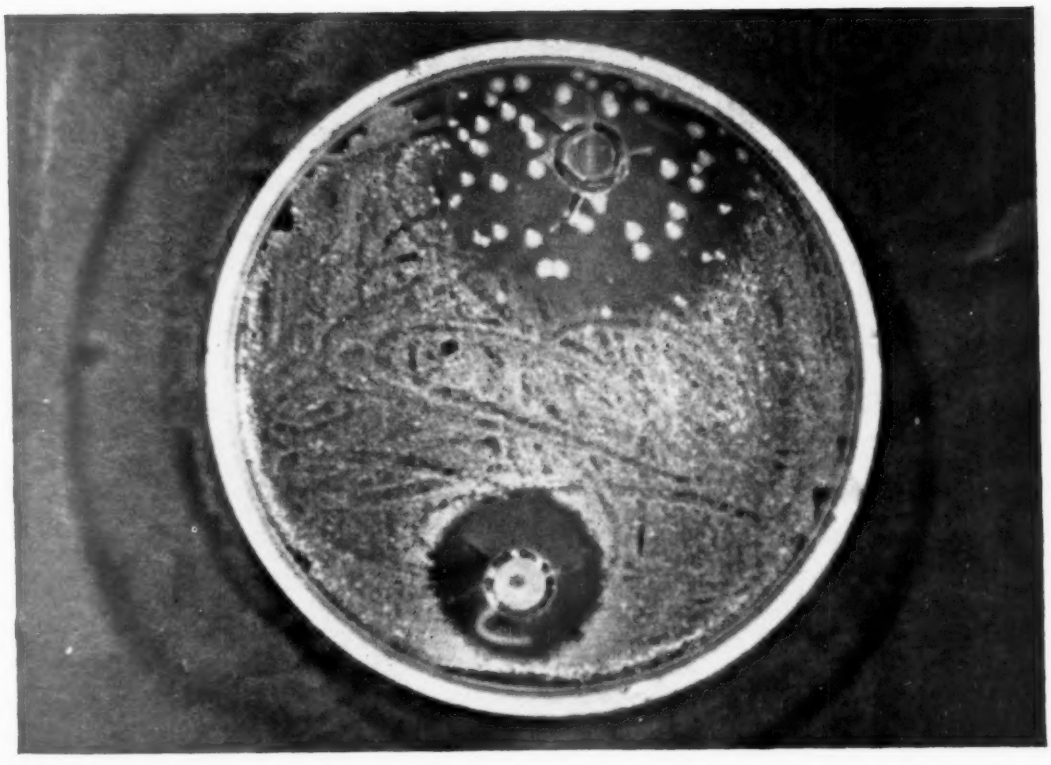


FIG. 2.—Culture plate (case No. 9) showing penicillin sensitivity test (above) with colonies of resistant coliform organisms.

TABLE 5

GROUP B: SULPHASUXIDINE ALONE

Case No.	Diagnosis	Clinical grade	General signs	Penicillin (units)	Suxidine g.	Alive	Dead
1	Right otitis media and nasopharyngitis	Mild	D, V, W	—	9·25	A	
2	Prematurity; condition deteriorating	Moderate	De, T, W	—	6·25	A	
3	Bilateral otitis media, nasopharyngitis, abscess of thigh and cellulitis of elbow.	Severe	D, V, W	50,000	12·25	A	
4	Right otitis media and nasopharyngitis	Moderate	W	225,000	15·25	A	
5	Bilateral otitis media and nasopharyngitis ..	Moderate	D, De, W	350,000	12·25	A	
6	Bilateral otitis media and nasopharyngitis ..	Moderate	W	175,000	12·25	A	
7	Prematurity; condition deteriorating	Severe	D, De, W	—	8·5	A	
8	Bilateral otitis media and bronchopneumonia ..	Severe	D, De, T, W, Cy	212,500	9·25		D
9	Bilateral otitis media and bronchopneumonia ..	Severe	D, De, T, W	250,000	18·25		D
10	Prematurity, bronchopneumonia and subdural haemorrhage.	Severe	D, De, W	—	6·25		D
11	Bronchopneumonia, jaundice	Severe	D, V, De, T, W	100,000	9·25		D
12	Prematurity, jaundice; condition deteriorating	Severe	De, W	25,000	6·25		D
13	Bilateral otitis media	Severe	D, V, De, T, W	150,000 100,000 200,000	12·25 — —	A	
14	Bilateral otitis media	Moderate	D, V, De, T, W	225,000 175,000	12·25 6·25	A	
15	Prematurity, jaundice; condition deteriorating	Moderate	De, W	—	6·25	A	
16	Bilateral otitis media	Severe	D, V, De, W	275,000	9·25	A	
17	Bilateral otitis media and nasopharyngitis ..	Mild	V, W	—	9·25	A	
18	Bilateral otitis media and nasopharyngitis ..	Moderate	D, V, W	200,000	9·75	A	
19	Left otitis media and nasopharyngitis	Moderate	D, V, De, T, W	—	9·75	A	
20	Prematurity, jaundice; condition deteriorating	Moderate	De, W	—	6·25	A	
						15	5

POST-MORTEM FINDINGS. The results of the post-mortem examinations were as follows. In four of the fatal cases the presence of bronchopneumonia was verified and in two confirmed by microscopic section. One of these was also found to have a small subdural haemorrhage and right acute otitis media. In the case of the fifth infant who died, bronchopneumonia was suspected in life but only bronchitis was found together with bilateral otitis media.

POST-MORTEM BACTERIOLOGY. Swabs from the right middle ear and lungs in case No. 10 grew coliform organisms, resistant to penicillin but sensitive to sulphonamide. In case No. 11 culture from the lung grew coliform organisms, resistant to penicillin but sensitive to sulphonamide. Swabs from the middle ear in case No. 12 grew coliform organisms, resistant to penicillin but sensitive to sulphonamide.

In this group it was intended to test the efficacy of sulphasuxidine. Only about 5 per cent. of this drug is absorbed (M.R.C., War Memo., No. 10) and it is active against organisms of the coliform group, causing a fall in the numbers of these organisms in the intestinal tract. Used alone it is not therefore likely to be of benefit in the type of infection under treatment, and in practice it was often found necessary to proceed to penicillin administration. In the above table where no penicillin is mentioned none was given. As sulphasuxidine was not given concurrently with the penicillin the following doses were employed: 0·75 g. as the initial dose, and then 0·5 g. four-hourly, to mature infants, and 0·5 g. as the initial dose and then 0·25 g. three-hourly to premature infants. Sulphasuxidine by itself was given a fair trial, the courses lasting three to six days and only if improvement was not manifest was penicillin given. Penicillin was on one occasion given in doses of 12,500 units daily (second course in case No. 14).

In this group nine were considered to be severely ill, nine moderately ill and two mildly ill. There were six premature infants, of whom two died.

SYMPTOMS. General symptoms were displayed as follows: diarrhoea 13, vomiting 9, dehydration 14, pyrexia 7 and loss of weight 20. Temperature lasted at most three days after treatment was begun, usually only one day, and varied from 99·2° F. to 104·8° F. In one case (No. 9) it rose again and remained uncontrolled. Loss of weight varied from 4 to 22 oz.

COURSE OF THE ILLNESS. Thirteen cases suffered from otitis media and in ten of these the administration of penicillin became necessary because sulphasuxidine had no apparent effect on the inflammation of the tympanic membranes. In two cases (No. 13 and 14) relapse took place even after penicillin, and in those who recovered the ears settled clinically in four to fourteen days after penicillin was given. Two of the thirteen cases

died (No. 8 and 9), and one of these developed bronchopneumonia the day after penicillin was begun; in the other the temperature settled, rose again, and remained uncontrolled. Penicillin had no effect on this case. In case No. 3 the infant was taken from hospital against advice when only a small quantity of penicillin had been given. This child also developed cellulitis of the elbow and an abscess of the thigh, and penicillin had had no effect at the time of discharge from hospital. Possibly in cases No. 3, 8 and 9 penicillin was given too late. The remaining three cases of otitis media (cases No. 1, 17 and 19) settled well with sulphasuxidine alone in four to five days, but in two an accompanying nasopharyngitis continued for a longer period. Two were only mildly ill and one moderately ill. The remaining seven cases of the group consist of six premature infants who were going downhill and one case of pneumonia, who had both sulphasuxidine and penicillin but unfortunately died. Of the six premature infants (No. 2, 7, 10, 12, 15 and 20) one had penicillin treatment for one day following unsuccessful sulphasuxidine therapy but died. One of those treated with sulphasuxidine alone died. Three responded very well to sulphasuxidine alone and another progressed well at first and latterly was pyrexial for no apparent reason but ultimately recovered.

The following cases in this group (No. 8, 9, 13, 14 and 16) are described in greater detail. In all but No. 8, only that part of the weight curve dealing with the illness is shown.

Bacteriology in Life. In nineteen instances bacteriological examination of the faeces showed no evidence of pathogenic organisms. In one case a specimen was not obtained. Urine examination in two cases was also negative. Pus from the abscess of thigh in case No. 3 grew Staphylococcus aureus.

Post-mortem Findings. In cases No. 8, 9, 10 and 12, the presence of bronchopneumonia was confirmed by microscopic sections. In case No. 8 right acute otitis media and mastoiditis were also found. The middle ears in case No. 9 were found to be normal, probably due to treatment, and the liver looked fatty but was normal on section. In case No. 10 bilateral acute otitis media, subperiosteal haematoma and subdural haemorrhage into the posterior fossa were also found and in case No. 12 right acute otitis media. Permission for post-mortem examination was refused in case No. 11.

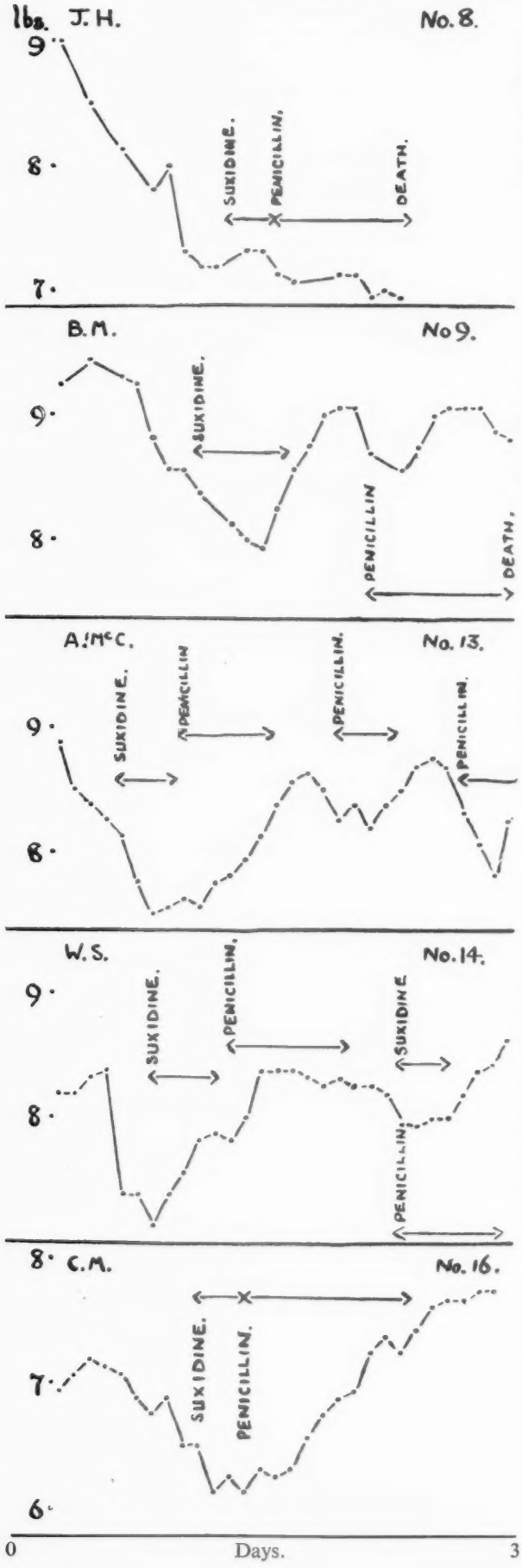
Post-mortem Bacteriology. Splenic culture in case No. 9 grew B. Coli. Direct smears from the middle ears in case No. 10 showed coliform organisms and Gram positive cocci while cultures from the ears and lungs grew coliform organisms, resistant to penicillin but sensitive to sulphonamide. Cultures from the lungs in case No. 12 grew coliform organisms, resistant to penicillin, and non-haemolytic streptococci, resistant to sulphonamide.

Discussion

The group treated with penicillin alone (Part I, Group A) is very disappointing and the good results reported earlier have not been maintained. This group contains a high proportion of premature infants, among whom the death rate was 72·7 per cent. Comparing this high figure with that for premature infants suffering from similar infections and treated with penicillin and sulphonamide, the death rate is 42·8 per cent., a considerable improvement. The virulence of such infections seems to reach its maximum in the early months of the year, when the present experiment was conducted, and this probably accounts for the difference in the results of the previously reported series treated with penicillin alone and the present group of cases treated with penicillin alone. The better results obtained by combining sulphonamide with penicillin constitute a strong argument for this mode of treatment. Burns and Gunn (1944) describe four cases of gastroenteritis, associated with otitis media and mastoiditis, two of whom received penicillin locally into mastoidectomy wounds, one intravenously and one, which developed pneumococcal meningitis, both intramuscularly and intrathecally. One of these cases who recovered also had sulphathiazole and three, one of whom died, had sulphamezathine. The combination therefore seems to give better results than penicillin alone.

The next problem is to decide which of the many sulphonamide drugs is the most efficacious. If the composition and severity of the groups described in the present series are disregarded, it appears that, of the two sulphonamides used, combination with sulphasuxidine gives the better results. The rationale of using sulphasuxidine in this way lies in the fact that it reduces the numbers of the intestinal coliform organisms (M.R.C. War Memo. No. 10). Coliform infections are peculiarly common in the neonatal period of life. Macgregor (1939), in her exhaustive account of neonatal pneumonias, found organisms of the colon bacillus group and Staphylococcus aureus the commonest pathogenic organisms. Both in the previously reported series and in the present series coliform organisms have been grown frequently, and possibly invasion by these organisms as the illness continues is a common happening. For example, in case No. 3 (Part I, Group A) the first nasal swab grew Staphylococcus aureus, sensitive to penicillin and sulphonamides, while the second, thirteen days later, grew coliform organisms, resistant to penicillin but sensitive to sulphonamide. On the other hand coliform organisms may militate against success in another way. Abraham and Chain (1944) found that B. Coli produces penicillinase which inactivates penicillin completely. Whatever may be the rôle of coliform organisms, any treatment calculated to reduce their number seems reasonable. Sulphasuxidine alone was on the whole unsatisfactory, although it is noteworthy that four out of five premature infants treated with sulphasuxidine alone recovered.

It can be seen from table 6 that the most dangerous and difficult case to treat is the premature infant with bronchopneumonia. The results in acute otitis media are very satisfactory indeed.



8. J. H., male, born 24–2–45, developed acute otitis media, with considerable loss of weight and cyanotic attacks. Suxidine had no effect on otitis media, and penicillin was begun, but little change in the ears was seen. Cyanotic attacks, probably due to bronchopneumonia, began before the otitis developed, but had ceased for some days. They began again during penicillin treatment.

9. B. M., male, born 9–1–45, developed acute otitis media with some weight loss. The inflammation of the tympanic membranes did not settle although suxidine was given for six days. Weight was regained but lost again with pyrexia and acutely inflamed drums. Penicillin caused some improvement, but the drums never became quite normal. Bronchopneumonia had developed meanwhile.

13. A. McC., female, born 30–3–45, developed otitis media and suxidine had no effect. Penicillin was given and improvement and gain in weight began. The ears settled clinically in six days. Unfortunately relapse occurred and further courses of penicillin were necessary. The infant did well after the third course of penicillin and was 10 lb. in weight when discharged from hospital

14. W. S., male, born 16–5–45, developed otitis media and some improvement occurred with suxidine, but the tympanic membranes did not become normal. When gain ceased, penicillin was begun and ears settled clinically in eight days. Relapse occurred and a combined course was given, when ears settled clinically in seven days and gain in weight was satisfactory. The fact that the curve remains flat after the first course suggests that the inflammation had not completely settled.

16. C. M., male, born 23–4–45, developed acute otitis media and suxidine had no effect. Penicillin was given with immediate improvement and gain in weight. The ears settled clinically in eleven days.

Only one myringotomy was necessary and no mastoid operations. This is a great improvement on treatment with sulphonamides alone, when the death rate was 14·1 per cent. and myringotomies and operations were frequent (Henderson and Couper, 1946).

TABLE 6

COMBINED ANALYSIS OF THE PENICILLIN AND SULPHASUXIDINE TREATED GROUPS

	Number	Deaths
Total	47	10 (21·2 per cent.)
Premature infants	17	7 (41·1 per cent.)
Mature infants	30	3 (10 per cent.)
Prematurity; condition deteriorating.	7	1
Prematurity and bronchopneumonia.	7	5 (71·4 per cent.)
Prematurity, bronchitis and nasopharyngitis.	2	
Prematurity, bronchitis and otitis media.	1	1
Bilateral acute otitis media and nasopharyngitis.	26	
Bronchopneumonia	1	1
Bronchopneumonia, otitis media and mastoiditis.	2	2
Bronchitis	1	

Conclusions

(1) The previously reported good results from treatment with penicillin alone during September, October and November have not been continued in the early months of the year, probably due to differences in the virulence of the infections.

(2) Better results are obtained by combining penicillin treatment with sulphonamide treatment.

(3) Two sulphonamides were tested, sulphathiazole and sulphasuxidine, and of the two, sulphasuxidine proved the better when combined with penicillin.

(4) Further investigation with other drugs of the sulphonamide group and with different doses of penicillin are necessary.

Thanks are due to Dr. H. H. Macwilliam, Medical Superintendent, Walton Hospital, Liverpool, for permission to publish this paper and to Prof. T. B. Davie, Professor of Pathology in the University of Liverpool and Distribution Officer of the Liverpool Medical School Penicillin Committee, for much helpful advice.

REFERENCES

Abraham, E. P., and Chain, E. (1944). *Brit. med. Bull.*, **2**, 16.
Burns, M. B., and Gunn, W. (1944). *Brit. med. J.*, **2**, 178.
Couper, E. C. R. (1945). *Arch. Dis. Childh.*, **20**, 117.
Henderson, M., and Couper, E. C. R. (1946). *Arch. Dis. Childh.*, **21**, 23.
MacGregor, A. R. (1939). *Arch. Dis. Childh.*, **14**, 323.
Medical Research Council (1943). *War Memorandum*, No. 10.

THE PSYCHOLOGICAL ASPECT OF ALLERGIC SKIN REACTIONS IN CHILDHOOD

BY

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The following study is based on the investigation of cases of allergic skin disorder in children and young adults which have been referred to me from the Dermatological Department of Guy's Hospital. All were cases which had received physical treatment for some time and were not improved. During my observations the physical treatment was not altered unless it was stopped altogether. Twenty-six cases were investigated; they included cases of infantile eczema, Besnier's prurigo, and two cases of papular urticaria. The word allergic is used as an expression of convenience to denote those symptoms such as eczema, asthma, prurigo, or papular urticaria, which may be produced in sensitive persons by foreign substances, but which, it appears, may also be produced by abnormal psychological states.

Barber (1929) has always emphasized the psychological aspect of allergic skin conditions, and in all these cases strong psychological factors were found. Not only, as Rogerson (1937) found in his investigation of a similar series of cases, did the children show psychological conditions which would have necessitated treatment, even if their skin condition had not been present, but there were marked family problems, and the child with the skin lesion was particularly involved. The presence of the parental problem would not seem strange in children referred for psychological difficulties, but it did seem strange in children referred from another department of medicine. It was also found that the problem was a complex one; not only were there the psychological disturbances responsible for the occurrence of the skin condition, but there were also those created by it both in the child and in the parents. In fact, a vicious circle was set up.

Appearance of the skin. In the cases of papular urticaria, small irritating papules appeared on any part of the body; they were transitory, and usually lasted only a few days, but they were recurrent. In eczema-prurigo the lesions occurred chiefly in the flexures; the wrists, ankles, the popliteal space, the flexure of the elbow and the face were commonly affected. The skin was thickened and lichenified from scratching, and at times there was considerable excoriation. In severe and long-standing cases these changes become widespread, the skin becomes tough and dry, and the body hairs are worn away with scratching; there may be no eyebrows, and the hair on the scalp may also be worn away. The finger-nails, and in some cases the toe-nails, become polished, and may be rubbed away so that the outer edges are concave, the nail-bed is sometimes exposed, and the tips of the fingers become very tender. In acute attacks there is eczematization of the affected parts, associated with fluid retention.

Methods of investigation. In all cases the mother was interviewed, and sometimes the father was seen. A careful history was obtained, and the parents reassured. Advice was given as to the treatment and management of the child at home, and, in some cases, the parents' own difficulties were discussed. In all cases, except that of a baby of five months, treatment was given to the child, but sometimes the parents also required treatment. Psychological treatment may so affect the child that it may no longer be susceptible to the parents' difficulties, and, though these difficulties still remain, the child may continue its development freed from symptoms.

The child was seen alone in a room specially fitted for the purpose. In this room is a sand-tray, water, some toys, such as dolls, trains, horses, and plenty of paper, pencils, crayons, paints, clay and plasticine, etc. The room should not be too tidy, so that it does not matter if the child spills anything, and it is usually advisable to have washable walls as the children often paint and smear on the wall. These children in particular have strong guilt feelings about dirt, and it is part of the treatment to relieve that guilt. A child's play and phantasy are as real to him as life, and in them he expresses symbolically his reactions and methods of dealing with life. The psychiatrist observes the play and phantasy, and so obtains an objective understanding of the child's difficulties, for the mother's account of what is wrong is always coloured by her own difficulties, and rarely gives a true picture. In addition to revealing his problems, the child develops new trends, and through them symbolically solves his problems. Thus the interviews in the play-room are both diagnostic and curative.

A factor of importance is the relationship between the psychiatrist and child; only if the child feels secure can he express his difficulties and still more solve them. The psychiatrist must be prepared to

accept whatever the child offers, whether it be expressions of pleasure or of anger, and so help him to overcome the fears that are so strong in these children. Already the child has encountered a block in his development by the unfavourable psychological atmosphere of his home, and energy does not stagnate; it is deflected into emotional and behaviour difficulties, which are usually fruitless efforts to overcome his problems, and which in these children are associated with scratching and various so-called allergic reactions. The child is not trained or taught in these interviews, but is given opportunity for his own creative development. Little interpretation is given, but the child is encouraged to live through his difficulties which are expressed in his play, paintings and phantasy.

Even in tiny children painting is a valuable means of expression; it was even used with much success by a little girl of one year and three months; when the children see on paper the result of their activities, they receive a great stimulus to development. The mother of one small girl said the child always scratched until the blood came, but that when she had seen the blood she ceased to scratch. In the play-room this child repeatedly stroked her skin with the brush, and then painted her arm red; she was very absorbed doing this, but afterwards she ceased to scratch herself. There was certainly some phantasy connected with the scratching and bleeding, but unfortunately she was too young to discover what it was. Older children talk about their play and their paintings, and in them it is possible to observe the progress of the treatment, and to correlate it with the improvement in the skin condition.

While the children were playing they did not scratch, but immediately they were frustrated or in any way upset, as for example when one child micturated on the floor and felt guilty about it, they began to scratch.

Constitutional predisposition. In a small majority of these cases there was a family history of a predisposition to allergic reactions. In ten cases this was absent, but this does not necessarily exclude it, as it may be unknown to the parents, and in one such case the mother developed a neurodermatitis when the child had recovered. Of the remaining cases in which it was present, five gave a family history of asthma in the predecessors, and in one of these there was also a history of hay fever; six gave a family history of allergic eczema, and in one of these the paternal grandfather suffered from eczema and the paternal grandmother from urticaria; one mother had previously developed a probable urticarial rash following a blood transfusion. The remaining four cases gave a history of skin reactions which are considered to have a neurotrophic origin. In two cases the fathers suffered with psoriasis; in one case the father developed alopecia areata following an accident, and the mother of the fourth case developed vitiligo after the death of her mother, for which she held herself responsible.

Thus it will be seen that, in many of these cases, there may be present a constitutional predisposition, and, wherever there is diminished resistance, there is always the possibility of an excessive response to stimuli.

The question, therefore, arises why were these particular children in the family group involved? It was because they were involved in the parents' psychological difficulties, and there were special causes for this; the position of the child in the family, the meaning of the birth to the parents, the special problem existing in the family at that time, and the personality of the child.

Position in the family. Of the twenty-six children investigated, four (15·4 per cent.) were the eldest children in the family, ten (38·5 per cent.) were the youngest children, and eleven (42·3 per cent.) were only children, and only one child (3·8 per cent.) occupied a position in the middle of the family. This latter child was in an isolated position in that her brother was five years older than she was, and her sister seven years younger. In all cases but three, no other sibling was known to have any allergic disorder. Of the three cases, one stepbrother, eleven years older than the patient, had had attacks of sickness on eating eggs but was now well; the sister of another patient had 'daffodil disease', and, in a family of two boys, the elder brother, now seventeen years old, had eczema as a baby; the younger brother, the patient, was now five years old, so that the two children may be described as only children with eczema.

In all but five cases the family consisted of one or two children. Only in two of the remaining five cases were there four children in the family, and one was the eldest child and the other the youngest child and only girl. In another family the patient was the youngest of six children, and in one family of three living children the child affected was the youngest and really the only child, as his brother and sister had been evacuated all his life, and he had rarely seen them. Thus these children all occupied a special position in the family which rendered them more susceptible to any psychological difficulty of their parents.

Illustrative Cases

Case 1. The patient is a girl now twenty-one, eldest of four children, who has suffered since she was nine months old from very severe allergic eczema with eosinophilia, and in whom the psychological features of the disorder are clearly shown. She reveals the typical personality of these allergic children, for she is highly intelligent, sensitive, determined and aggressive. Her mother was a paranoid woman who had been a certified patient in a mental hospital for a short time. The marriage was a success for the first year, as the husband had had an amputation of the leg and his wife acted as nurse to him, but the marriage was no longer a success when the husband ceased to be an invalid. The girl was born about this time. At nine months she began to scratch. The father then confessed to his wife that he had had eczema, and that it could be traced back to his grandmother. Henceforth, the wife held him responsible for the girl's illness; he

felt guilty, and, to relieve his guilt, spent his time trying to cure her eczema. The father and mother had severe disagreements about the doctors she saw, the father was constantly examining her skin, and, in fact, after she came under my care, when he did not see her so frequently, he counted the pots of ointment that she ordered from the chemist. As a result of this, she has been unable to develop her own personality; she was never thought of as an individual, it was her skin that received the attention. The mother, unhappy in her own life, involved her daughter in it, and told her, even as a small child, her difficulties with her husband. After leaving a boarding-school the girl lived at home, and was a day student at the University. What individuality she had acquired at school was now gone; having no friends and no life of her own, the mother must know all her daughter's friends, criticize and destroy the friendships, even do her studies with her, intruding in everything. The eczema, always more or less present, became progressively worse until the daughter became an invalid, spending most of her time in bed, unable to see anyone because of the severity of the eczema. This patient was admitted into hospital when I first saw her. She made some improvement while in hospital, and it was considered inadvisable for her to live at home. It was decided that she was to take up residence at college, continue her studies, and have psychological treatment. Eventually she went home for a few days to make preparations for the new term, and at once there was a recrudescence of the eczema. It was then decided to readmit her to hospital in a few days' time; the father telephoned this to her at home one morning, and by evening the rash had ceased to weep and was improving. While the daughter was in hospital the mother became jealous of her husband visiting the girl, who became involved in a quarrel that developed between the parents, and immediately the eczema recurred. The patient is now living away from home and enjoying a normal life. The eczema-prurigo has practically disappeared. There was a gradual improvement during psychological treatment, but there have been exacerbations. For example, one occurred when her mother interfered with her holiday arrangements, attempting to decide whom she should visit and what train she should catch; another when she was bored with the monotonous routine at college and did not want to attend; a third after she spent a day in town with her mother. She is now able to stay at home with her parents without any relapse.

An interesting feature of the case is that the eczema appeared immediately after the causal incident, but when she discussed this with me the exudation disappeared within a few hours, and the reaction subsided. In addition to the skin lesion, there was increased fluid retention and diminution of urinary output at these times.

Her menstruation started at the age of fourteen and for two years was perfectly normal. As the eczema became worse the periods were irregular and scanty, and there were intervals of amenorrhoea for as long as six months. The periods have again become regular and normal as she has improved, showing the interaction of the psychological state, the endocrine system and allergic reactions.

This girl reacted to life's difficulties with an attack of eczema and this in itself cut her off from life. The treatment aimed at freeing her psychologically from her family so that she could develop her own personality.

Parental problems. The guilt of the parents is a striking feature in these cases. The problem of the parent becomes constellated in the child and the parents try to cure themselves by their behaviour to the child. Often they go from doctor to doctor, putting on lotion after lotion, and trying many and various kinds of treatment, and this in itself tends only to aggravate the child's difficulties.

Case 2. The mother of one little boy, J. S., was a childish, immature woman although she was twenty-nine years old. The youngest of her family, she always clung to her mother, and, after marriage, to her husband, who, however, was sent abroad ten weeks after the birth of the child. When the child developed eczema her whole problem was intensified. She was childish, and she felt very guilty, and thought she had failed somewhere; she neither wrote to her husband about the child's skin condition nor did she tell her parents who lived nearby. She avoided people as much as possible, and, if attention were drawn to the child's condition, she said it was a teething rash. She concentrated on trying to cure it, saying, 'I wash him in Lysol and he's always quite clean,' and, justifying herself, 'I have brought him up according to the rules of the Welfare Centre and this is the result.'

Case 3. Another example of the guilt of the mother resulting in her concentration on the skin affection to the extent that both the child and the parents attempted to remove the skin disease and so her psychological problem, is shown in the case of a boy of seven years old (B. E.). He was referred to the Department because he had a morbid interest in his skin. He suffered with weekly attacks of urticaria, and he picked the papules out of the skin. It was found that he was an illegitimate child, and that the mother had later married a man who was not the father of the child, but who was devoted to him, and ultimately adopted him. The mother was extremely guilty about this boy's birth, even more so when the child of the marriage was a still-born monster. She thought the skin disease was something terrible, probably a venereal disease, and resulted from his illegitimacy; she and her husband spent hours at night rubbing ointment on to his skin in a hopeless attempt to cure it. The child improved considerably with psychological treatment, and the mother became relieved of much of her guilt. For reasons connected with the war the treatment, however, had to be interrupted, but the mother wrote to say that he has only had two slight attacks in three months, and she was sure these were due to his nerves because the first one occurred on the first night of the flying bombs, and the second when she told him he was to be evacuated.

Case 4. In the case of G. W., a little boy of two years, the father, who is now in the Navy, had obsessive ideas about dirt, rashes and health. These ideas were stimulated when the child developed a rash, and this added to the mother's difficulties. The mother was a lonely, isolated woman, in a state of considerable depression. The patient was a fifth child, two having died, and the other two being evacuated and scarcely seen by the mother since the war. The mother did not want this fifth child, and had taken every means to procure an abortion. Her own mother suffered from delirium

tremens, and her father, to whom she was devoted, left her mother, so that she was placed in an institution away from her brother and sister. As a result of her early environment, she was unable to show any real feelings; she had rejected her other children, and rarely spoke to her neighbours, and had no friends. She was afraid of criticism and felt inferior to everyone. Now very depressed, she had many fears and irrational moods in which she would punish the child unmercifully. The absence of the father increased her loneliness and intensified her depression, and the child received the full brunt of her severe neurotic state. She frequently said she wished she had never had him, and yet, in her anxiety about him, she gave up doing her housework during the day so that she could always be with him. She would not allow him to mix with other children as she said the mothers would think the rash infectious. Thus she projected the whole of her problem on to the child, who was not able to develop normally in this atmosphere. The most important thing was his eczema, which caused her such anguish, and on which all her attention was focused. She watched him all the time to see if the eczema was coming out.

The problems of the parents are of infinite variety. It is not any particular problem, and it may involve the mother or the father, but usually it is the problem of both parents. In its early years the child is dependent physically and psychically on the mother and is, therefore, susceptible to her difficulties, but it can also be affected by the father's problems affecting the child through the mother.

Case 5. In the case of G. H., two years old, the mother was a passive, feminine person, warm and with much feeling, and she was genuinely fond of the child. The father was a cold, intellectual type, who was not really interested in the children, and who married because his mother had died and he had no home. As is very common, particularly in this country, the mother felt inferior to her husband, as he was an intellectual type, and she was much more a feeling type, and was not intellectually developed; even when he was courting her he would sit and read a book instead of paying attention to her. He was not interested in the first child, who was like him in type; he did not want any more children, and he has not taken his share in the responsibility of them. The mother loved children, and wanted another. A boy was born, and the mother was apprehensive from the first, for she thought boys were like their mothers and girls like their fathers, so that the boy would be like her. He was like her, loving and affectionate. The mother had had eczema as a baby, and when a few weeks old this child developed spots which, at seven months, developed into infantile eczema, the father said it was her fault for wanting another child, her own inferiority increased, and the child had to bear all her negative side. When first seen the boy was two years old, and he was suffering with severe eczema; he clung to his mother, and cried and tore at his skin when separated from her. Not only did the mother try to stop him from scratching, but the father smacked him for it, and he was prevented not only from scratching but from developing in a normal way. The atmosphere is clearly shown by his little sister of six years old who said, 'No, no Geoffrey,' in her sleep. He improved a little after the first few treatments, and even slept without having his hands tied, but the air raids caused lack of sleep to the family, and the mother, already in a state of nervous exhaustion, became much worse. The child was affected by her nervous state, his eczema became so severe that he scratched until the blood poured down his face, and he had to be admitted to hospital, for it was feared that the mother might do anything to him in her desperation. Within four days his skin had practically cleared after receiving only one psychological interview, and the physical treatment being continued as at home. The day after he was admitted to hospital the mother became ill with a quinsy, and there can be little doubt that the illness was connected with her psychological state. The child was transferred to another hospital for administrative reasons and, while he was there, he developed pemphigus, but he never made any attempt to scratch these lesions. The mother was seen in the Psychiatric Out-Patient Department while the child was in hospital, and her feelings of inferiority and identification with the boy lessened to some extent. As soon as he returned home the eczema broke out again slightly, but he attended the Child Guidance Clinic regularly and the rash was kept under control and gradually faded. As he improved, the mother improved too, the father began to take more interest in him, and the whole atmosphere in the home became more normal. The skin has remained in good condition, and the child's personality continued to develop in spite of the flying bomb attacks, which were very severe in the district in which he lives.

Case 6. It has been found that improvement in the children may cause an improvement in the psychological state of the parents, but occasionally improvement in the child seems to have intensified the parents' problem. A little girl, M. W., of three years old, with eczema-prurigo, was an unwanted child, born about five years after the last of three boys. The mother, a hard, rigid woman, constantly quarrelled with the father, who married for the first time when he was forty-five, and wished to continue his bachelor existence in the home. He refused to sleep with the mother as he said the child's scratching kept him awake all night. The mother unconsciously hated the child, who, feeling this, clung to her, and demanded her constant attention. With psychological treatment the child's skin affection disappeared, but it was quite impossible to alter the home conditions. The child slept alone, and was no longer an ostensible cause of the parents' differences. These, however, remained. The mother's problems could no longer be projected on the child, and the mother herself developed a neurodermatitis. Later the child had a slight recurrence of the eczema, and it was found that the parents were now fighting in front of her. In fact, one day the mother said the child was not so well, and when I looked at the mother she had the largest black-eye I have ever seen.

Case 7. In another case, B. K., aged six, the mother developed an unconscious resistance when the boy began to improve, but later she also showed evidence of improvement. Both the mother and child were of a lower level of intelligence than is usual in these cases, the boy falling in the dull group on the intelligence scale. The mother was immature and unable to show her feelings, and consequently she had a strong will to power. The father was strongly tied to his mother; he visited

her before his wife when on leave, and was unable to make any decision without consulting her. Relations between the parents have always been very poor, and they have never talked things out or attempted to make a success of their married life. In addition, the mother also had a poor relationship with her father, and even married to spite him as he forbade the marriage owing to the bad medical history of her husband's family. She was pleased she was going to have a child, but wanted a girl. The labour was difficult, a boy was born whom she said 'looked like a terrible piece of jelly' and she was very disappointed. She was unable to face the situation from the beginning. As soon as she got up she was unable to feed the child as she said her legs 'locked.' Her relations both with her husband and her father have been poor and full of resentment, and she has identified her son with both men; she is irritable with him, and says she 'takes it out of him.' Under these conditions the child was cross and irritable from the beginning, and, at three months, he developed eczema of the buttocks which spread over the body, and has never cleared. He was a shy, inhibited little boy, but after three attendances the prurigo considerably improved. At this stage an incendiary bomb fell through the roof of his bedroom, and he immediately had a severe recurrence of the eczema and of the asthma, from which he also suffered. It was the hole in the roof which caused him the severest shock, and this incident increased his insecurity so that, for a time, he became more strongly tied to his mother. As he improved, his mother found him increasingly difficult to handle; he was becoming less burdened by her unsolved problems, and able to find his own adaptation to life. At this time she said her 'legs locked' as they did after his birth, and she could not bring him to hospital for treatment for some weeks, and, when she did, she leaned heavily upon him. However, this was only a passing phase, and, with the boy's psychological and physical improvement established, she also began to look much happier, younger and prettier.

It appears that these children always have a tendency to react to life's difficulties with an allergic attack. The earlier and more thoroughly the psychological difficulties of both the parent and child are treated, the less likely is the allergic reaction to become a fixed mechanism in the child's reaction to life. The importance of the psychological treatment is to free the child from the burden of the parents' problems so that he can develop his own personality. He can then deal with life by normal methods and not by an allergic attack which acts as a means of defence against life.

Case 8. A baby of five months, R. K., with infantile eczema, illustrates the effect of the psychological atmosphere at home. The child had suffered with infantile eczema since he was three months old. He was referred from the Skin Department with a note saying that his mother was in a state of panic. She was a young woman of twenty-one who was living with her mother, and her husband was serving in the Navy. She was an immature young woman who had never had to face any responsibility; in fact, her mother referred to her as 'my baby.' This was the first child, and the mother was so guilty about the eczema that she did not tell her husband about it; however, he returned unexpectedly on leave, but showed no anxiety about it, and said it was hardly noticeable. Eventually she brought the child to the Dermatological Department at Guy's Hospital; at the second attendance it was found that the child's skin had not improved, and she was in such a state of panic that she was referred to the Psychological Department. At this interview she was given some reassurance after the discussion of some of her own difficulties, and subsequently the dermatologist reported that the child was improved. The father then returned home for a long leave, the mother was happy, and the child continued to improve. A few weeks later, however, the mother again returned to the hospital in a state of great panic, saying that the child's skin was as bad as ever. It was found that, four days previously, the father had returned to the Navy, and, two days later, the grandmother had met with an accident. The child's eczema became worse on the following day.

Case 9. The picture is quite different if the mother is able to deal with her problems. The mother of a little girl was an intelligent, educated young woman, who had herself suffered with eczema and in whom there was a strong family predisposition. At about six months the baby developed redness and irritation behind the neck and knees. The mother realized the condition and its implications. The father had been sent abroad for some years a few weeks after the birth of this, the first, child, and the mother went to live with friends, where she felt frustrated and not herself. When the child developed eczema she did not pay unnecessary attention to it, but at once moved to a more happy environment, saw that her own life was more full and happy, and that the child had every opportunity for a normal development. For some time the child had red patches which became much more obvious when she was upset or angry, but they gradually disappeared. She only scratched a little in the more acute stages. The child is now a healthy little girl of three years old with no sign of eczema; in temperament she is a typically allergic child, intelligent, sensitive, aggressive and determined.

Case 10. A boy of two years, P. C., when first seen suffered with eczema-prurigo. He had not yet established clean habits, and had severe behaviour difficulties. He was a very determined child, and consequently not easy to bring up. His mother was an ambitious woman, and regretted that she had not been able 'to take up scholarship.' When he was born she had given up her post as optical glazier and was evacuated to the country. She was unhappy in many billets, her mother, with whom she never agreed, came to live with her, and her husband joined the Army. She thought that her present unhappy state was due to her inability to develop her intellectual qualities, and she projected this on to the child who, she said, had been 'a nuisance since birth.' It was more probable that she would never have realized her intellectual ambitions, for she had not the ability to do so. They were compensations for her inability to act as a mother and a woman. She and her mother disagreed about the bringing up of the child, and the child himself had a difficult personality, but with psychological treatment his behaviour difficulties and eczema cleared up. Adjustments were made so that the mother now had a home of her own,

and became more satisfied with life, but when her mother came to stay with them, she became unhappy, and the child's behaviour difficulties and eczema returned. When the grandmother left the behaviour difficulties cleared up, but psychological treatment was necessary to clear up the eczema. Later the maternal grandmother again visited them, and again there was some recurrence of the eczema and behaviour difficulties, but this time it was of a much less marked degree.

Case 11. The mother of a baby girl of a year and three months, J. S., had married secretly, since her own mother, who was a dominating, possessive woman, forbade the marriage. After the marriage the mother refused to acknowledge her daughter, who felt guilty about the position, for she was fond of her mother, though she realized the necessity of what she had done. Her husband was an over-virtuous, neurotic person, who would not allow her to say anything against her parents, and so reinforced her sense of guilt. It seems her mother told her she would spend her time at hospital with the children, and she was in despair when she had to attend hospital with the little girl, first with eczema and then with asthma as well; she felt that it was a judgment upon her for what she had done. The father was of a very worrying disposition, who even listened to the child's breathing when she was sleeping peacefully in case it stopped, and was afraid to allow the child to sleep in a room alone. Some advice and reassurance was given to the mother, but the main treatment was directed to the child. In the short time during which she attended, six interviews, she began to walk and to talk, the eczema disappeared, and she has had no further attacks of asthma. Her mother said the child appeared to become more intelligent, and there has been no relapse since the birth of another child.

Case 12. In the case of J. W., aged three years, both parents were nervous people, and the father had developed alopecia areata following an accident some years before. The mother, eldest of seven children, had always been her father's favourite child, working with him in the flour mills and being his constant companion when he went to the cinema, etc. Her first child was born in the first year of the marriage and the small family had a happy time together, often visiting the country at week-ends in the motor-bicycle and sidecar. Then the husband fell out of work, the rent of the house suddenly increased, and the wife found she was again pregnant. The husband would not let his wife work, but found a small house in a lonely part, and gradually their savings dwindled. After the happy early years of her married life, and the background of her father's constant companionship, she was now living a lonely life with a husband who had become moody and often did not speak to her for long intervals. The second child was born and at four months developed eczema. This added to her depression, and eventually the child was sent to hospital as the mother developed a severe state of nervous exhaustion. While in hospital the skin became infected, and the child was ill for a long time. Eventually she returned home, and, as the eczema had not improved, the mother brought her to the Dermatological Department of Guy's Hospital, whence she was referred to the Psychological Department. The home circumstnaces had now improved, the mother was better, and was not unduly worried about the eczema, but, though the family problem had cleared up, the child was still suffering from its reaction upon her, and treatment was necessary to free her from its influences.

Case 13. D. W., aged eight years, was a bright, intelligent, affectionate girl with eczema-prurigo and asthma. She had a very strong relationship to her father, who had always wanted to be a doctor. He was invalided from the Army with a duodenal ulcer, and trained as a chiropodist and masseur. He had a very willing patient in his daughter, and tried many varieties of ointment on her skin. Recently he bought a stethoscope, and has given her breathing exercises, listening to her chest before and after the exercises. He has also given her massage to her back which, she says, she finds very soothing. When she first came to the clinic her skin was much lichenified, and she wheezed continuously. I have advised him that doctors do not usually treat members of their own family, and he has agreed to leave the treatment to me. Her progress is now continuous and satisfactory, and, fortunately, the father's work as a chiropodist keeps him very busy. The concentration of the parent on the child's eruption fixes it in her mind, and she is not likely to become free of something that gives her father so much interest and pleasure and makes her the centre of so much attention.

Dermatologists have noted that discussions with the parents are frequently disagreeable, and might interfere seriously with the welfare and physical treatment of the child. The reason for this is that the problem of the parent is so much involved. It is usually unconscious and so is their weak spot; it needs careful and tactful handling. The fact that the parents' problems are unconscious needs special emphasis. Frequently the parents do not know that these problems exist, and they are consciously doing their best for the child. When a person is unconscious of his difficulties he should not be blamed.

Personality and psychological difficulties of the child

With one exception all the children in this series had an intelligence well above the average. They were determined and aggressive, and egoistical to the point of narcissism. (The first patient even dreamed that she looked into a pool of water to see the bottom, but all she saw was her own face; she said it was 'like Narcissus.') They were also very sensitive children, and this seems to be an important point in their constitution which makes them so susceptible to the psychic influence of their parents.

In addition, they had many fears and were thus insecure; this, I believe, is partly due to their sensitivity, and partly to the effect of their parents' difficulties upon them. The children are very self-conscious about the skin condition; they feel different from other children, and are very guilty. As their psychological state improved so also did the eczema. Their feeling of guilt and insecurity makes them difficult patients to treat. When faced with difficult or disagreeable situations they are

likely to have an immediate relapse of their symptoms. The young girl of twenty-one first cited denied a certain unpleasant fact in the course of treatment rather than admit her fault. She rectified it at the next visit, but the conflict was sufficient to produce a slight but definite attack of eczema. On taking up her post she came into a situation in which she might be subjected to criticism, and she told me that the tingling of her skin was almost irresistible, and she had the greatest difficulty in not scratching. Another fact which should not be overlooked is that these patients derive considerable pleasure from scratching and rubbing, and this also tends to isolate them, so that they seek pleasure in themselves rather than in the world around them.

It has been stated that the infantile eczema tends to clear up when the child is eighteen months to two years of age. In two cases I have observed at this age, the eczema cleared up when the child began to walk and could take more interest in its surroundings and express itself in them.

Conclusion

There are two operative factors present in the allergic skin reactions of childhood. The first is a constitutional predisposition to allergic manifestations in the child itself. The second is the presence of a psychological problem in the parents, affecting the child on account of special circumstances. These circumstances are the personality of the child, the problem which is created in the family, the position of the child in the family, and the meaning of the birth to the parents. It might be expected that separation of parent and child might cure the child, but this is not in fact the case. The child is affected not only on account of the atmosphere in the home but also on account of its own personality, and it is found that the child itself needs treatment.

Psychological treatment is given to the child, and, in some instances, to the parents as well. When the child improves, the parents may improve too; in other cases the parents' difficulties may get worse as they cease to project their problems on to the child. With treatment the child is able to develop so that he is no longer affected by the parents' troubles. It is essential for the child to receive psychological treatment; physical treatment alone merely transfers the allergic reaction from one system to another, as in the case of a child who was free of eczema for three months following injection treatment, but at once developed asthma; the eczema later recurred, and her psychological problems had remained untouched.

The feeling of guilt of the parents is an important factor and complicates the other psychological factors. Not only is the parental problem connected with the outbreak of the skin affection, but there are psychological difficulties caused by it both in the parents and in the child.

It is clear that such morbid reactions as eczema, prurigo or papular urticaria, the tendency to which may be inherited or acquired early in life, are likely to produce a profound effect on the personality of the child. Whatever the particular symptom may be, it represents the child's reaction against an unfavourable environment or mental shocks. The earlier and more thoroughly the psychological difficulties of both parent and child are treated, the less likely is the allergic reaction to become a fixed mechanism in the child. He can then deal with life by normal methods rather than by an allergic reaction which serves as a defence against life.

References

Barber, H. W. (1929). *Lancet*, **2**, 591.
Rogerson, C. H. (1937). *Quart. J. Med.*, **6**, 387.

THE STATISTICS OF PREMATURITY

A PLEA FOR STANDARDIZATION

BY

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A standardized method of presenting statistics on prematurity is the only sure foundation on which to build reliable scientific data regarding this major paediatric problem. Hitherto, it has not been possible to compare the prematurity statistics emanating from maternity hospitals, owing to the lack of a uniform method of statistical analysis. To enable accurate comparisons to be made between various methods of care and treatment it is suggested that the following seven conditions would provide a comparative basis:

(1) A large number of infants.
(2) Accurate weighing at birth.
(3) Strict interpretation of the definition 'live-born.'
(4) Inclusion of all liveborn infants with congenital malformations.
(5) Definition of the weight range of viable prematurity.
(6) Subdivision of the standard weight range into half-pound weight groups.
(7) Segregation of the infants of booked mothers from those of unbooked mothers.

1. **A large number of infants.** Conclusions which are statistically significant can be drawn only from a large series of consecutive cases. There should be several hundred, preferably 500 or more. The importance of this becomes more apparent when the need for subdividing premature infants into several standard weight groups is appreciated, since, as a result of such subdivision, the proportion of infants in the lighter weight groups is small, and figures relating to small numbers are statistically insignificant. Table I shows the number and the percentage of infants in each half-pound weight group in each of six consecutive years, and in the aggregate, at the Simpson Maternity Hospital, Edinburgh. It is apparent how much more widely the figures vary from year to year in the lighter weight groups, where there are relatively few cases, than in the heavier weight groups where the numbers are much larger. The danger of drawing false conclusions from small series of cases has recently been emphasized by Crosse (1945).

2. **Accurate weighing at birth.** Sensitive, accurate weighing machines are essential for recording the birth-weight of premature infants, if accurate definition of the standard weight range and accurate allocations into standard subdivisions are to be attained. The birth-weights of infants born in

TABLE.

THE INCIDENCE OF LIVEBORN INFANTS WITH A BIRTH WEIGHT OF 5½ LB. OR LESS, IN EACH ½ LB. WEIGHT GROUP, IN EACH OF THE YEARS 1938 to 1943 AND IN THE SIX-YEAR PERIOD, AT THE SIMPSON MATERNITY HOSPITAL, EDINBURGH.

Year	Weight group in pounds																		Total no. of infants
	5½–5 incl.		4.15¾–4½		4.7¾–4		3.15¾–3½		3.7¾–3		2.15¾–2½		2.7¾–2		1.15¾–1½		1.7¾–1		
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
1939	73	34·9	39	18·7	28	13·4	21	10·0	18	8·6	12	5·7	10	4·8	8	3·9	0	0	209
1940	86	36·9	47	20·2	35	15·0	28	12·0	16	6·9	10	4·3	7	3·0	4	1·7	0	0	233
1941	111	41·7	46	17·3	39	14·3	19	7·1	14	5·3	16	6·0	14	5·3	8	3·0	0	0	267
1942	92	35·7	59	22·5	38	14·7	23	8·9	17	6·6	15	5·8	11	4·2	3	1·2	1	0·4	259
1943	92	34·7	60	22·6	41	15·5	24	9·0	19	7·2	12	4·5	10	3·8	1	0·4	6	2·3	265
1944	96	36·0	45	16·8	45	16·8	28	10·5	24	9·0	14	5·2	5	1·9	9	3·4	1	0·4	267
1939–1944	550	36·7	296	19·7	226	15·0	143	9·6	108	7·2	79	5·3	57	3·8	33	2·2	8	0·5	1,500

large maternity hospitals, only, can be accepted as reliable. In many small maternity hospitals and in most nursing homes various types of inaccurate and unreliable weighing machines are employed.

3. **Strict interpretation of the definition 'liveborn.'** The necessity for rigid interpretation of the definition of a liveborn infant requires emphasis, because it is a great temptation to classify infants who die within a few minutes or hours of birth as stillbirths, and thus improve the neonatal mortality figures. It is a common practice in the United States and elsewhere (Barnes and Willson, 1942) to exclude from the category of liveborn infants all those who die within twenty-four hours of birth. Since the mortality in premature infants, particularly in the lighter weight groups, is concentrated in the first day of life, strict interpretation of the definition of a liveborn premature infant, as defined by the American Academy of Pediatrics (1935), is a statistical necessity. The definition reads: 'A premature infant is one who weighs 2,500 g. or less at birth (not on admission) regardless of the period of gestation. All liveborn premature infants should be included, evidence of life being heart-beating or breathing.'

In the seven years period 1938–44 at the Simpson Maternity Hospital, Edinburgh, 489 infants who weighed 5½ lb. or less at birth died in the hospital; 48·9 per cent. died within 24 hours of birth and 24·1 per cent. within 6 hours of birth. These figures prove the absolute necessity for strict interpretation of the definition 'liveborn' if prematurity statistics are to have any scientific value.

4. **The inclusion of all liveborn infants with congenital malformations.** All liveborn infants with congenital malformations should be classified as livebirths, even if the malformation is regarded as being incompatible with survival. This point requires emphasis in the interests of statistical accuracy, because it is a common practice to eliminate liveborn infants with congenital malformations judged to be incompatible with survival from the category of livebirths (Barnes and Willson, 1942). Since the prognosis regarding survival depends to a considerable extent on personal opinions, it is highly desirable that this factor should be eliminated by classifying all liveborn infants with congenital malformations, however severe, as livebirths.

5. **Definition of the weight range of viable prematurity.** A standardized weight range of viable prematurity would provide a common statistical basis. This is a fundamental necessity where figures embracing all premature infants, without division into subgroups, are given; though it is not so essential where the subdivision of premature infants into numerous standard weight groups is practised.

THE MAXIMUM WEIGHT STANDARD. At the present time this is the only universal weight standard of prematurity. The definition reads—'A premature infant is one who weighs 5½ lb. (2,500 g.) or less, at birth, regardless of the period of gestation.' This standard was first advocated as a suitable international standard by Ylppö in 1919, and it was soon generally adopted on the European Continent. It was officially recognized by the American Academy of Pediatrics in 1935 (Hess and Lundeen, 1941), although it had previously been adopted by numerous American workers, and it was officially recognized in Great Britain in 1938 (*Brit. med. J.*, 1938). The adoption of this universal upper-weight standard of prematurity has proved of great statistical value. Paediatricians have found it much more satisfactory than the estimated incomplete period of gestation standard, which formerly had been the standard of prematurity in general use.

The old definition has three main disadvantages: (1) The frequent uncertainty regarding the date of onset of the last menstrual period. (2) The frequency with which infants estimated to be premature weigh 6 to 7 lb. or more. (3) The frequency with which infants estimated to be mature weigh 5½ lb. or less.

The new definition has two main advantages: (1) The weight of 5½ lb. constitutes an appropriate dividing line between infants who are clinically mature and those who are clinically immature. Those who weigh more do not require special nursing care, whereas those who weigh less do require it. (2) Exact correspondence between the avoirdupois and metric systems in round figures does not occur at any other point in the neighbourhood of 5 to 6 lb. This is the principal reason for the adoption of the weight standard of precisely 5½ lb. (2,500 g.).

A MINIMUM WEIGHT STANDARD. The adoption of a universal minimum weight standard of prematurity is highly desirable. Numerous workers have recognized this fact and various standards have been suggested and used by them, but no official recommendation regarding a minimum weight standard has yet been made. Some workers have used a standard of viability of 1,000 g. (2 lb. 3·2 oz. whilst others prefer a standard of 1,500 g. (3 lb. 4·8 oz.). Various standards between these two extremes have also been suggested. A minimum weight standard of 2¾ lb. (1,250 g.) was recently suggested by myself (Henderson, 1945) as being the most suitable lower weight standard of viable prematurity. The figure of 2¾ lb. was shown to correspond approximately to an estimated gestation period of 28 weeks, the generally accepted age at which the foetus is presumed to become viable. The problem of attempting to find the average weight of infants, at the twenty-eighth week of gestation, was approached by analysing the relationship between the birth-weight and the estimated period of gestation in 1,041 liveborn single premature infants born in the Simpson Maternity Hospital in the six-year period 1938 to 1943. To endeavour to achieve a true relationship twin infants totalling 252 were excluded from the whole series of 1,293 liveborn infants who weighed 5½ lb. or less at birth, because twin infants weigh less than single infants of the same foetal age. Stillborn and deadborn premature infants were also

excluded from the calculation, because the relationship between the weight and the foetal age is very variable in these circumstances owing to the frequency of gross congenital defects and intra-uterine death.

In the series of 1,041 single liveborn premature infants there were 44 infants in the 3 to 2½ lb. weight group with an average gestation period of 28·9 weeks, and 34 infants in the 2½ to 2 lb. weight group with an average gestation period of 27·7 weeks. These figures seemed to point to a lower weight limit of viability of between 2½ lb. and 2 lb., but, as pointed out at the time, there is an important reason why the average weight of infants of 28 weeks gestation cannot be accurately calculated from hospital records. It is dependent on the general practice of regarding many infants who have a gestation period of 26 to 28 weeks as viable, and recording them as having an estimated gestation period of over 28 weeks to enable the mother to receive her maternity benefit. Such a practice seems quite justifiable, because the duration of gestation is only an approximate estimation and it is certainly right that the mother should receive the benefit of any doubt in borderline cases. From the statistical point of view, however, this practice vitiates the figures relating to the lower weight groups of premature infants, as a considerable number of pre-viable infants are notified as viable. It was concluded, therefore, that the figure of 28·9 weeks exceeded the actual period of gestation in the 3 to 2½ lb. group, and that the average weight of infants of 28 weeks' gestation probably lies somewhere between 3 lb. and 2½ lb.

It appeared from the above evidence that the most suitable universal minimum weight standard of viability which can be based on the generally accepted '28 weeks' gestation period' standard of viability is the weight of 2¾ lb. (1,250 g.). There are three good reasons why a birth-weight of 2¾ lb. should be accepted as the most suitable minimum weight standard of viable prematurity. They are: (1) The average weight of infants of 28 weeks' gestation appear to lie between 3 and 2½ lb. (2) The weight of 2¾ lb. avoirdupois corresponds exactly with the weight of 1¼ kg. (1,250 g.) in the metric system, a correspondence in round figures which is unattainable at any other point in the neighbourhood of 3 to 2½ lb. (3) The minimum figure of 2¾ lb. (1¼ kg.) is exactly half of the maximum figure of 5½ lb. (2½ kg.). This simplification has the virtue of making the minimum standard easy to remember, as the maximum standard is now well known and in general use.

LIVEBORN PRE-VIABLE INFANTS. Official adoption of the proposed minimum weight standard of viable prematurity of 2¾ lb. would necessitate the provision of a separate category for liveborn infants with a birth-weight of less than 2¾ lb. The term 'pre-viable' would suitably describe this category. Where prematurity figures are considered as a whole it seems desirable that this group of extremely premature infants should be placed in a separate category, because their chances of survival are remote, and it seems both unjustifiable and scientifically unsound to include these infants, who practically speaking are non-viable, in the same category as infants who have a reasonable chance of survival. The recognition of such a category along with the proposed minimum weight standard would encourage obstetricians and registrars in maternity hospitals to be more forthright, and to present figures more in accordance with the facts, than is often the case to-day. At present, there is a reluctance to include extremely premature liveborn infants which do not survive in the general prematurity figures, and an inclination to classify them as abortions. This practice is quite understandable, but it is highly to be deprecated on statistical grounds, and manifestly unfair to those maternity units in which an honest attempt is made to be accurate by including all fatalities among liveborn premature infants, however small, as neonatal deaths.

A total of 118 liveborn infants with a birth weight of less than the proposed minimum standard of viability of 2¾ lb. were born in the Simpson Maternity Hospital, Edinburgh, in the six-year period 1938 to 1943. The total of liveborn infants with a birth-weight of 5½ to 2¾ lb. inclusive born in the same period was 1,286. Thus, of 1,404 liveborn infants with a birth-weight of 5½ lb. or less, 91·6 per cent. would, according to the proposed standards, be classified as premature infants (birth-weight 5½ to 2¾ lb. inclusive), and 8·4 per cent. would be classified as pre-viable infants (birth-weight less than 2¾ lb.). Only 4 of the 118 'pre-viable' infants survived. This is a poor survival-rate and better figures are attainable (Cross, 1945). Nevertheless, even in the most ideal circumstances, the death-rate in infants with a birth-weight of less than 3¾ lb. will always remain very high.

WEIGHT STANDARDS OF PREMATURITY AND STILLBIRTH CLASSIFICATION. Stillborn and deadborn premature infants should also be defined as those infants with a birth-weight between 5½ lb. and 3¾ lb. inclusive. A pre-viable category is unnecessary in the case of stillborn infants, as those with a birth-weight of less than 2¾ lb. are, of course, classified as abortions.

The substitution of a minimum weight standard of 2¾ lb. for the customary standard of an estimated gestation period of 28 weeks, would reduce considerably the proportion of premature stillborn infants falling into the category of viable stillborn infants, and increase correspondingly the proportion falling into the category of abortions. The effect of the change of definition in the six-year period 1938 to 1943 at the Simpson Maternity Hospital was as follows: There were 520 stillborn infants which weighed 5½ lb. or less and which were estimated to have a gestation period of 28 weeks or more (i.e. premature by current standards); 139 (27 per cent.) of these weighed less than 2¾ lb. and would be classified as abortions by the 5½ to 2¾ lb. standard of viable prematurity. Thus a

much larger proportion of stillborn infants than of liveborn infants would be eliminated from the category of viable prematurity if the 5½ to 2¾ lb. standard were to supersede the 5½ lb. to 28 weeks' standard, and would henceforth be regarded as abortions. The great difference in the proportion of liveborn and stillborn premature infants who would be classified as pre-viable, instead of viable, is explained by the fact that the average weight of stillborn infants is considerably less than the average weight of liveborn infants at a corresponding period of gestation. The principal causes of the lower average weight of stillborn infants are the common occurrence of gross congenital malformations, such as anencephaly, and of intra-uterine death.

The considerable reduction in the number of premature stillborn infants which would follow the adoption of the 2¾ lb. standard of viability would appear to be desirable, because a large proportion of the foetuses which would fall into the pre-viable (abortion) group would show either gross congenital malformations or maceration following intra-uterine death, and should not under any circumstances be classified as viable. In the series of 520 premature stillborn infants previously mentioned, 29 per cent. of the foetuses, which the proposed minimum standard would eliminate from the category of viable prematurity, showed gross congenital malformations, principally anencephaly. Accurate figures relating to intra-uterine death cannot be given, but at least 20 per cent. of those eliminated would probably fall into this category.

COMMENT. A strong case for the adoption of an international minimum birth-weight standard of prematurity would appear to emerge from the foregoing evidence. There is nothing new in the conception of a standard of viability. The standard in general use is that of an estimated gestation period of 28 weeks, and it would seem highly desirable on scientific grounds to institute a common denominator for both the maximum and minimum limits of prematurity. As the maximum weight standard of 5½ lb. (2,500 g.) has been proved to be a highly desirable reform, it is surely logical to urge the acceptance of a minimum weight standard of viable prematurity to replace the existing standard with which it corresponds.

6. **Subdivision of the standard weight range into standard half-pound weight groups.** Subdivision of the standard weight range of prematurity (5½ to 2¾ lb. inclusive) into several standard weight subdivisions is essential for statistical purposes, because the definition embraces premature infants ranging between those who are slightly premature and those who are extremely premature and have just become viable. Further, the proportion of infants of various weights may vary greatly in different series of cases and it is valueless to compare premature infants of widely differing birth-weight.

It is not possible to achieve exact correspondence in round figures of the avoirdupois and metric systems for several subdivisions of the standard weight range. The best that can be achieved is to divide the avoirdupois range of 5½ to 2¾ lb. into five ½ lb. subdivisions and one ¼ lb. subdivision as follows: 5½ to 5 lb. inclusive, 4 lb. 15¾ oz. to 4½ lb. inclusive, 4 lb. 7¾ oz. to 4 lb. inclusive, 3 lb. 15¾ oz. to 3½ lb. inclusive, 3 lb. 7¾ oz. to 3 lb. inclusive, and 2 lb. 15¾ oz. to 2 lb. 12 oz. inclusive; and the metric range of 2,500 to 1,250 g. into five 250 g. subdivisions as follows: 2,500 to 2,250 g. inclusive, 2,249 to 2,000 g. inclusive, 1,999 to 1,750 g. inclusive, 1,749 to 1,500 g. inclusive, 1,499 to 1,250 g. inclusive. The five ½ lb. subdivisions do not quite correspond with the five 250 g. subdivisions, as the five ½ lb. groups cover a range of ¼ lb. less than the five 250 g. groups.

The varying proportion of viable premature infants in each half-pound weight group from year to year in the Simpson Maternity Hospital series reviewed is shown in Table I.

7. **Segregation of the infants of booked mothers from those of unbooked mothers.** The term 'booked' refers to mothers who arrange early in pregnancy, without recommendation, to have their confinement in hospital; whereas the term 'unbooked' refers to mothers who are admitted to hospital as obstetrical emergencies, or are recommended for confinement in hospital because of ill-health, obstetric or otherwise, in the present or in a previous pregnancy, or because of multiple pregnancy. The separation of these two groups of cases into separate categories is a fundamental statistical necessity, for the prognosis of the infant is much better (in the aggregate) in booked than in unbooked cases. Nevertheless, this point is usually ignored. If the proportion of booked and of unbooked cases was the same in all maternity hospitals it would not be necessary to make this distinction, but such is far from the case. No unbooked cases are admitted to some maternity hospitals, whereas such cases constitute a substantial minority of the total cases admitted to others.

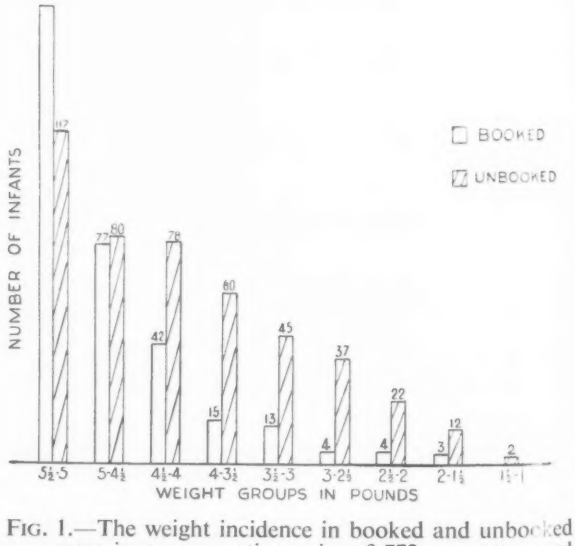

FIG. 1.—The weight incidence in booked and unbooked cases in a consecutive series of 772 premature and pre-viable liveborn infants, born in the three-year period 1942 to 1944 at the Simpson Maternity Hospital, Edinburgh.

In the three-year period 1942 to 1944 at the Simpson Maternity Hospital, there were 772 liveborn infants (596 single, 166 twins and 10 triplets) with a birth-weight of 5½ lb. or less; 41 per cent. of them were born of booked mothers and 59 per cent of unbooked mothers. As approximately 80 per cent. of the mothers during this period were booked, the incidence of liveborn infants with a birth-weight of 5½ lb. or less was 4·7 per cent. in the booked category and 2·71 per cent. in the unbooked category. The number of premature infants in each ½ lb. weight group in this series is shown separately for each of the two categories in

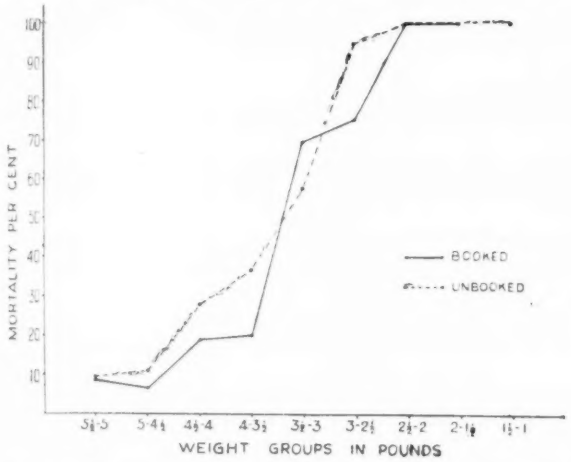

FIG. 2.—The mortality in booked and unbooked cases in each ½ lb. weight group in a consecutive series of 772 premature and pre-viable liveborn infants, born in the three years period 1942 to 1944 at the Simpson Maternity Hospital, Edinburgh.

the diagram in fig. 1. This shows a preponderance of booked cases in the heaviest weight group of 5½ to 5 lb., about an equal number in the two categories in the 5 to 4½ lb. group and a great preponderance of unbooked cases in all the lighter weight groups. The variability in the proportion of booked and unbooked cases in successive weight groups would be unimportant if the mortality in the two categories was approximately the same in each weight group, but such is far from being the case. The mortality rate for all liveborn premature infants (viable and pre-viable) in the booked cases of the series was 15·4 per cent. and in the unbooked cases it was 35·5 per cent. The frequency of antepartum haemorrhage and of toxaemia in unbooked cases are the principal reasons for the much poorer prognosis in that category. The comparative mortality in each ½ lb. weight group is shown graphically in fig. 2. In each of the three important weight groups 5 to 4½ lb., 4½ to 4 lb. and 4 to 3½ lb., together comprising 46 per cent. of the total cases, the unbooked cases showed twice the mortality of the booked cases.

Clearly it is statistically essential to analyse the infants born of booked and of unbooked mothers separately, because (1) there is a great difference in the weight distribution in the two groups, and (2) the prognosis is much poorer in the unbooked cases, particularly in the three important intermediate weight groups ranging from 5 lb. to 3½ lb.

Summary

The necessity of adopting a standardized method of presenting statistics on prematurity is emphasized.

Seven conditions which would provide a satisfactory statistical basis have been suggested.

REFERENCES

Barnes, A. C., and Willson, J. R. (1942). *J. Amer. med. Ass.*, **119**, 545.

Brit. med. J. (1938). **1**, 1011.

Crosse, V. M. (1945). *The Premature Baby*, London, 136–7.

Henderson, J. L. (1945). *J. Obstet. Gynaec.*, **52**, 29.

Hess, J. H., and Lundeen, E. E. (1941). *The Premature Infant*, Philadelphia, 1.

Ylppö, A. (1919). Z. Kinderheilk., **24**, 1.

MALNUTRITION IN CHILDREN UNDER THREE YEARS OF AGE IN ASHANTI, WEST AFRICA

BY

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At a time when problems of food supply are prominent in all parts of the world, a clinical account of malnutrition in young children in Ashanti may be of more than local interest.

Ashanti lies in West Africa, north of the Gold Coast. Kumasi, the capital, is situated in the tropical forest belt, with roads radiating from it in all directions. A Welfare Centre was opened in the town fifteen years ago to provide medical care for children and for pregnant women. At this centre there were last year over 50,000 attendances, and cases of under-nutrition and malnutrition were frequently seen. Although the two conditions tend to merge, it is with the latter that this article deals.

Background. The people live in small villages of mud-walled houses in forest clearings, and even the town dwellers constantly go and come from ' bush.' Food is supplied by the small subsistence farms, which are cultivated with the hand hoe after the undergrowth has been cut and burned. Soil fertility is maintained by shifting cultivation only, and the chief crops are maize, plantains, and roots—the roots being mainly cassava and cocasia antiquoran. Maize is eaten fresh-roasted at harvest, but is more often stored to make porridge, after it has been ground and partly fermented. Plantains and roots form the basis of most meals, of which there are two a day, and are eaten after boiling, or more often after boiling are beaten to a dough-like substance or ' fu-fu ', and eaten with a pepper sauce containing vegetables.

Of domestic animals none larger than sheep and goats survive, on account of the prevalence of tsetse fly. These animals are a form of wealth; they are eaten only on special occasions, and they are not milked. Fowls are used in much the same way. Eggs, being potential chickens, are rarely eaten. Meat is supplied irregularly by hunters; fish is imported smoked and sun-dried, but it is too expensive to be used by most of the people except as a flavouring.

Thus, to summarize the food position, no milk is used for children except the mother's; protein is in short supply, especially for the children, who are served after their elders; and carbohydrate, of poor quality according to Clarke (1932), forms the bulk of each meal.

Malaria is endemic, and mainly of the subtertian variety. Worm infestation is common, particularly ascariasis.

In those surroundings, however, the baby, once he has survived the hazards of birth, starts life fairly well. Breast feeding is universal, and is continued for eighteen months, two years, or longer, unless the mother becomes pregnant again. Most women have ample milk for six months at least, and as the child grows he begins to eat bits of starchy food thrust into his hand. He may or may not be given maize porridge, but whenever he cries he is always offered something to eat.

When the infant becomes a toddler he fares well or ill according to the amount of care given by the mother and according to the severity of the malaria from which almost all children suffer. At this stage there is marked lack of protein in the child's food, and probably only continued breast feeding tides him over a critical period. When he begins to move about by himself ascaris infection takes place, and enteritis from various causes is common, so that his condition tends to be below par. Nevertheless, to the untrained eye the toddler between one and three years does not look undernourished, and indeed may appear plump. Frequently, however, this appearance of well-being is deceptive, because although subcutaneous fat is present, there is often also slight general oedema. This generally passes unnoticed, and spontaneous cure is the rule as the child becomes older and better able to fend for himself. In cases of definite malnutrition oedema is more marked, and swelling of the hands and feet may be the first sign to attract the mother's attention.

History. The history in a developed case of malnutrition is unsatisfactorily vague as to prodromata, but certain points are generally found common to all. The child had been healthy at birth and had done well for eighteen months or two years, i.e. up to the birth of the next child. Illness of the displaced baby is so common that there is a general belief among the people that the unborn child exerts a direct and malign influence upon his brother, and the latter is often, therefore, sent to stay with relatives. When finally the mother comes to the clinic for advice, she appears with a plump baby on her back and the ex-baby hardly able to walk. Any history of precipitating illness other than that of ' fever ' (malaria) is indefinite,

and the variety of symptoms complained of is as interesting as it may be misleading, ranging from diarrhoea to swelling of the hands and feet or face, worms, cough, loss of appetite, rumbling in the stomach, and in more advanced cases, inability to walk. For whichever symptom the mother is concerned about, she wishes to be supplied with a bottle of medicine.

Condition on examination. The patient is a toddler and under three years of age. The appearance is characteristic, and with some practice even early cases can be recognized. The child does not look thin, partly because subcutaneous fat is present and partly because of general oedema. The latter may be so slight as hardly to pit on pressure, but it gives to the child's cheeks a typically heavy and

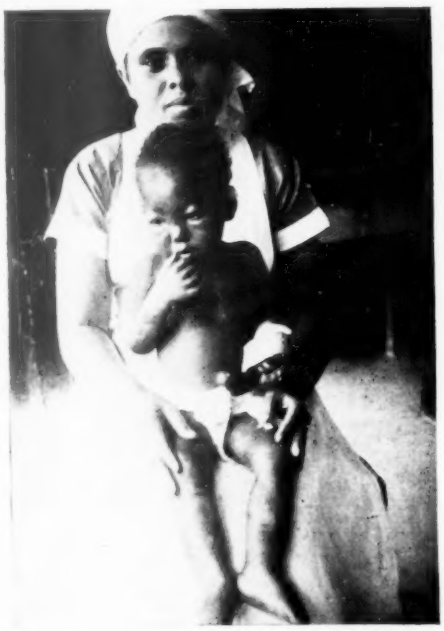

FIG. 1.—Case of malnutrition, taken one week before death.

slightly pendulous appearance. Pitting can as a rule be made out over the shins and on the backs of the hands and feet. In spite of the stolid appearance, the child is irritable and cries readily when examined. He sits down or supports himself as if his legs were weak, and in fact, muscular tone is very poor. Ankle and knee jerks are absent. The hair is sparse, brown and dry, and the skin is dry, with crazy-pavement markings most distinct where oedema is most marked. Small ulcers are often present on the legs and buttocks. In the mouth, ulcers, thrush, and redness and soreness of the tongue are common. The abdomen is blown out, and the mother states that the child has diarrhoea. Blood and mucus are generally found in the stools, also ascaria ova and flagellates. The pulse is rapid, but cardiac enlargement has not been demonstrated. Cough, probably due to oedema, is generally present. There may be an enlarged spleen, and malaria parasites may or may not be found in the peripheral blood. Anaemia is always considerable, with haemoglobin (Talquist) of 5 per cent. or less. The red cell picture is that of dimorphic anaemia as described by Trowell (1942) in East Africa. The temperature is not raised unless active malaria or other infection is present. The urine not infrequently contains albumen, and casts are sometimes found.

Prognosis. The prognosis depends upon how soon correct treatment is instituted. In all except early cases, unless treatment in hospital is agreed to, the child goes steadily downhill, and dies often as a result of some terminal infection. Of recent years the outlook in hospital has become more cheerful, now that the all-important place of diet in causation and treatment has been recognized. But no means has as yet been found of assessing which case will respond to treatment and which will not do so. Excessive and persisting oedema with albumen are bad prognostic signs, while early and steady reduction of swelling with early disappearance of albumen are hopeful. In all cases, however, relapse is common.

Differential diagnosis. Once the child has been surveyed as a whole there is no particular difficulty in diagnosis. The absence of definite localizing signs, the scanty hair, oedema and unhealthy skin are all helpful pointers. The medical officer must beware of being side-tracked by individual signs and symptoms, and of overlooking the fundamental malnutrition. Only drastic revision of the child's diet will save the child's life, if it can be saved.

Treatment. Little is gained by the treatment of symptoms unless and until the need for a suitable diet has been recognized and dealt with. Because of the unhealthy state of the digestive tract, food must be bland and easily digested. At the same time it is important that local food-stuffs should be utilized as far as possible, so that relapse may be avoided when the child is discharged from hospital and has to return to ordinary family foods. From one's knowledge of how deficient these foods are in protein, the aim has been at once to supply an easily obtained and easily digested form of protein. To this end the local gruel made of fine-ground and fermented maize, with milk and eggs added, forms food which is easily taken. Soups made from bone stock and with finely mashed liver are also given from the first. Vegetables and coarser carbohydrates are added as improvement takes place. The only foreign constituent used is tinned milk.

VITAMINS. The results from giving individual vitamins either by mouth or by injection have been found by the writer disappointing on the whole, a conclusion which is in line with other work along the same lines (Richards, 1945). Vitamins B1 and C have sometimes been observed to have produced a temporary diuretic action which has not, however, led to permanent improvement. Nicotinic acid does not appear to have any specific action. Riboflavin may perhaps have some effect in helping to clear up sore mouth. Crude liver extract, such as Campolon, has been found useful in cases which

have been in hospital for a time and are at a standstill. Cod-liver oil has not been available during the war, and the local palm oil, though rich in carotene, has an undesirable laxative action. One of the most distressing features of the condition is diarrhoea, and for this symptom drug control has not been found effective. It clears up as general improvement takes place.

PLASMA. Among the cases treated by the writer it was possible to treat only one child with intramedullary plasma. The dose given was a small one, and no permanent good results were observed. This, however, may be a form of therapy worth urther trial.

Next in value to careful feeding, the most important single factor in bringing about recovery is good nursing. These children should be guarded against chill, and the unhealthy skin must be cared for. Oiling with the local palm-kernel oil appears to be useful for this purpose.

If oedema persists for a week or so, more drastic measures sometimes meet wih gratifying results. The diuretic, 'Neptal', has been used, in doses of 0·3 c.c. subcutaneously, and after one dose the child's whole appearance may change overnight, with disappearance of most of the oedema. If the tissues fill up again, a second dose may result in permanent relief. In unfavourable cases the diuretic appears to produce no effect.

As soon as the oedema begins to disappear mental improvement is striking, and for the first time the child begins to sit up by himself and to take some interest in his surroundings. Appetite improves gradually, but it is some time before the diarrhoea subsides. The blood and mucus in the stools generally disappear shortly after admission, and are undoubtedly largely due to the irritant enemata to which the child has been subjected before admission. Genuine gain in weight does not occur until the patient has been in hospital for some time, and progress is often checked, with temporary increase of oedema. When the oedema has finally been relieved the extreme flabbiness of the child can be appreciated; arms and legs are thin, and of a soft, dough-like consistence, with a marked lack of muscular power.

As general improvement progresses the unhealthy superficial layers of the skin darken and flake off, the hair begins to grow and darken, and the condition of the mouth clears up. In unfavourable cases the oedema increases, the child becomes more drowsy, is more difficult to feed, and slowly fades out, unless carried off by some terminal infection.

Comment

How far malnutrition and under-nutrition may be considered as separate entities is rather difficult to say, and undoubtedly the one tends to merge into the other. The malnourished child, with his failing health and strength, eats less and less, and gets even less than his normal share of the important foods, which in any case are in short supply, so that a vicious circle is set up. The child may finally be eating nothing but a little starch.

Clinically, the condition seems to be identical with the 'Kwashiokor Disease' in the Gold Coast Colony, described by Williams (1933), but the writer has not found it to be associated with a maize diet, and in the few cases examined post-mortem, liver damage was not so extensive as Williams found it in that disease. In uncomplicated cases death in hospital seldom occurs, but in two cases recently examined, the livers, though extensively vacuolated, were by no means diffluent.

The clinical picture is interesting when compared with reports from other parts of the world, for example, with the report on nutrition in Newfoundland (Med. Survey, 1945) where the basic rations are very different.

Improvement, and reduction of incidence, can only be expected as knowledge of causation spreads and as the standard of living is raised.

Summary

Malnutrition as seen in children in Ashanti after weaning is described.

The condition is associated with low protein diet, and is distinguished by the occurrence of oedema, unhealthy skin and hair, sore mouth and diarrhoea.

The line of treatment is indicated.

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REFERENCES

Clarke, A. (1932). *Trans. Roy. Soc. Trop. Med. Hyg.*, **26**, 3.
Trowell, H. C. E. (1942). *Afr. med. J.*, **19**, 268.
Richards, M. B. (1945). *Brit. med. J.*, **1**, 433.
Williams, C. D. (1933). *Arch. Dis. Childh.*, **8**, 48.
Med. Survey Nutr. Newfoundland (1945). *Can. Med. Ass. J.*, **52**, 227.

THE INCIDENCE OF CONGENITAL PYLORIC STENOSIS

BY

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The present investigation was undertaken in order to determine, with as much precision as possible, the incidence of manifest congenital pyloric stenosis in the United Kingdom. The conclusion reached is that this incidence is in the order of three per thousand live births.

The term 'manifest' requires some explanation. There is evidence, given by Wallgren (1937), Malmberg (1939), Bexelier (1939) and Lewis (1944), that the anatomical deformity of pyloric stenosis may be present without symptoms. Clinical experience suggests that such an occurrence is rare, but no estimate of frequency can at present be made. Further, there are cases of pyloric stenosis in which the symptoms are so mild that the diagnosis is not made, and which undergo spontaneous cure without treatment. The frequency of such cases, again, can not be assessed accurately, though it is probably low. The remaining cases of congenital pyloric stenosis—those which appear to form the vast majority—are those in which symptoms, once initiated, are for some time progressive, and which, without treatment, recover only after a prolonged illness or else die. It is to such cases that the term 'manifest' is here being applied.

In an attempt to determine the frequency of congenital pyloric stenosis an endeavour has been made to trace all cases occurring in Newcastle-on-Tyne infants born during the years 1939 to 1942 inclusive. The conditions in Newcastle are peculiarly favourable to an investigation of this type, especially in regard to numbers involved and to the clinic and hospital arrangements. A local knowledge of these conditions justifies the view that almost every case of manifest congenital pyloric stenosis, as defined above, does at some stage reach one of four hospitals or one of a number of nursing homes, and the figures shown below have been obtained by a scrutiny of the records of these four hospitals, and from replies to a questionnaire sent to the nursing homes. It is known from the report of Spence and Miller (1940) that no case of congenital pyloric stenosis died at home in Newcastle during the year 1939. Care has been taken to include only 'Newcastle babies', that is infants born to Newcastle parents; no baby born in Newcastle of parents not resident in Newcastle has been included. In this way the number of cases can be related directly to the number of births for Newcastle in the same period. The validity of the figures rests finally on the diagnostic criteria by which cases have been included in or rejected from the series. In all but two of the cases included the diagnosis was confirmed by operation; in each of the remaining two the history was typical, visible gastric peristalsis was present, a pyloric tumour was palpable, and gastric lavage showed evidence of considerable gastric retention. The criteria of rejection are more difficult to state. Most of the cases (36 out of 49) were admitted to one hospital; at this hospital the writer has examined all the in-patient and out-patient records of the years in question, and found it unnecessary to reject any case in which the clinical picture was suggestive of pyloric stenosis. At a second hospital, which yielded 11 cases, all in-patient records were examined, with a similar result; very few babies were treated as out-patients at this hospital during the years of the survey. It was known to the writer that relatively few cases of pyloric stenosis were treated at the third hospital, and in this no records were examined except those of infants diagnosed as pyloric stenosis; only one Newcastle case was found, and there were no 'doubtful' cases. At the fourth hospital an examination of the admission register revealed no cases of pyloric stenosis, but it was customary over the period surveyed for any infant reaching the hospital with a suspicion of pyloric stenosis to be transferred to the first hospital mentioned. The figure for the nursing homes is based purely on replies to a questionnaire; only one case was reported.

The total numbers of cases from these sources were, for the years 1939, 1940, 1941 and 1942 respectively, 10, 16, 7 and 16. During these same years the numbers of live births to Newcastle parents were 4,599, 4,454, 4,115 and 4,289 respectively. Thus, out of 17,457 live born infants to Newcastle parents, 49 are known to have suffered from congenital pyloric stenosis, an incidence of 0·28 per cent. ($\pm$0·08 per cent.).

There is no statistically significant difference between this figure and the estimate of 0·40 per cent. given by Wallgren (1941) for Götheberg over the years 1934 to 1940 inclusive, his figure being based on 102 cases out of 25,642 live births. (The standard error of the difference between 0·28 per

cent. of 17,457 and 0·40 per cent. of 25,642 is 0·06 per cent.).

The importance of an estimate of this type is partly scientific and partly practical. Congenital pyloric stenosis is a condition which is, to a large extent, determined genetically (Cockayne and Penrose, 1943), and one would expect racial differences in incidence. As most reports from Latin America are of single cases, it may be presumed that the incidence there is much lower than in the United Kingdom, and Wallgren (1941) quotes Vilen as stating that pyloric stenosis is extremely rare in African native infants. These, however, are but impressions; they can be confirmed or refuted only when figures of incidence from these countries can be compared with those of Wallgren and those presented here.

From the practical standpoint, it can be argued that, as there are at present approximately 600,000 live births in England and Wales each year, any comprehensive medical scheme should offer facilities for the treatment of between 1,200 and 2,160 cases of congenital pyloric stenosis annually. That such facilities are not now available is suggested by a consideration of mortality figures. During the years 1939, 1940, 1941 and 1942 respectively, 335, 360, 389 and 359 deaths were registered as being due to congenital pyloric stenosis. Assuming the higher incidence figure, 2,160 cases annually, an average of 360 deaths indicates a case mortality of 16 per cent.; the incidence may well be below this maximum figure, giving an even higher mortality figure.

Summary

Arguments are given for considering the incidence of congenital pyloric stenosis in the United Kingdom to be in the order of three per thousand live births. This figure is not significantly different from that given by Wallgren for Sweden.

The writer is indebted to Dr. Percy Stocks for the mortality figures, and to the Staffs of the Newcastle hospitals and nursing homes for their co-operation.

REFERENCES

Bexelier, G. (1939). *Acta Pediat.*, **25**, 29.
Cockayne, E. A., and Penrose, L. S. (1943). *Ohio J. Sci.*, **43**, 1.
Lewis, F. L. K. (1944). *Brit. med. J.*, **1**, 221.
Malmberg, N. (1939). *Nord. Med.*, **4**, 3553.
Spence, J. C., and Miller, F. J. W. (1940). 'Report of an Investigation into the Causes of Infantile Mortality in Newcastle-upon-Tyne during the year 1939.' Newcastle-upon-Tyne.
Wallgren, A. (1937). *Svenska lak. tidning.*, **34**, 635.
——(1941). *Amer. J. Dis. Child.*, **62**, 751

DENTAL FLUOROSIS

BY

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The following account is given to demonstrate how dental fluorosis in a particular locality presents itself to the casual observer. The teeth of a boy first attracted attention on account of their dark brown discolouration. The staining resembled that of nicotine, but on closer examination proved to be too dark to be attributable to smoking in a boy, whilst the boy's fingers were not stained. On enquiry, the local inhabitants attributed the condition to 'iron' in the water, remarking that teeth in the district were bad: they tended to chip and rot early.

Opportunity shortly afterwards presented itself to examine some 150 children, representing between a third and a half of the whole school population, when special attention was paid to the condition of their teeth. The writer had not previously met with some of the lesions presented, but a description of the condition in a recent issue of the British Medical Journal suggested that they were those of fluorosis. Standard medical textbooks which were to hand contained no reference to the condition. Accordingly sketches (reproduced below) were made at the time, and have since been confirmed from the descriptions of McKay (1916) and subsequent writers. The age distribution of the lesions is shown below (fig. 1).

The lesions took the following forms:

1. HYPOPLASIA OF DENTAL ENAMEL. **(a)** The enamel was extremely thin but smooth, and in places deficient, leaving small circular bared areas of dentine varying from 1 to ¼ mm. in diameter. The larger ones might have been punched out with an ophthalmic trephine—if that were possible—so clean cut and regular were the edges. This lesion occurred unaccompanied by any other.

(b) Pitting: Small pits with sloping edges were scattered over the outer surface of the front teeth. Often they were seen as a single or double horizontal row. The biting edge of the other teeth tended to be ragged but the central incisors had a worn straight cutting edge. This appearance was recognized as significant of rickets and acute infections during the first year of life, which conditions were extremely prevalent in this locality. Thus the lesion on account of its mixed etiology had to be disregarded. A third but rare condition giving a similar appearance is that of partial agenesis of enamel (Sprawson, 1942).

2. DECALCIFIED AREAS. These were irregular patches of opaque white enamel. Clearly circumscribed patches occurred with mottling and pitting. But in other cases the patches covered the surface of the tooth and their edges were diffuse. They showed up as a dull white in contrast to the translucency of normal enamel. Disorders of calcium metabolism during early infancy frequently give rise to the former appearance, but the latter is more typical of fluorine intoxication.

3. MOTTLING. The enamel was unequal in thickness, forming ridges which were frequently arranged horizontally. This again is not typical of fluorosis but of any condition which interferes with the development of the enamel organ.

4. 'BROWNIN' or patches of brown stain, which reached a depth of chocolate in colour, appeared superficial and were confined to the outer surface of the upper front teeth below the lip line. This is the

No of children examined		a	b	2. Mottling	3. Decalcification	4. Brownin	No of children showing lesions
		1. Pitting					
3-5 yrs	22	-		-	-	-	-
5-7 ''	33	-		1	-	-	1
7-11	75	2		7	5	8	16
11-14'	17	-		3	3	4	6

FIG. 1.—Showing the Age Distribution of the various types of lesion noted.

typical lesion of fluorosis and when fully developed is diagnostic. Congenital syphilis can produce a muddiness, which might simulate mild cases. Hereditary opalescent dentine is apparently similar in appearance but affects all the teeth (Sprawson, 1942). Both conditions are, however, rare.

Other Characteristics of the Group. There was a tendency for the condition to occur more frequently among those children who showed evidence of previous rickets. The figures were small and not conclusive. Pillai, Rajogopalan. and De (1944) showed that in rats it is possible to suppress the lesions with an increased calcium intake.

Of the whole sample only four children showed any evidence of dental caries. This was scarcely surprising since these were a primitive people living largely on a vegetable diet, and as Crighton-Brown (1892) pointed out the fluorides contained in coarse milled flour limit caries.

Filling out of the lumbar curve was observed in two children, both showing some malnutrition but neither dental lesions. In England Kemp (1942) was unable to find any definite X-ray evidence in children of the osteo-arthritis and spondylitis noted by Miller and Roholm among adult cryolite workers.

Endemic goitre was conspicuous in the locality. It has been pointed out by Wilson (1941) that the two conditions tend to coexist. An iodine estimation of the water, however, was not possible.

The Locality. The area in question was a small village, ' Lauro', situated on the edge of the Naples plain, some twenty-five miles from that city. It was in this region that fluorosis, originally known as ' Denti Neri ' on account of the stain, was first recognized by the Italian physician Stephano Chiaie and later by Eager (1901).

The village is some twenty miles from Mount Vesuvius and the whole area volcanic. Roholm (1937) summarizes the results of six geological surveys done in the plain between 1910 and 1926. Fluorine was found in the following forms : HF, K_2SiF, and KBrF, which differ from those found in England, where the important compound is Fluorapatite ($3P_2O_8Ca_3$, CaF), and from those in Greenland, where it is Cryolite (Na_3AlF_6). Samples of rock were examined spectroscopically but the typical bands shown by Churchill (1931) were not seen. Another specimen was sent to the Geological Survey, London, for miscroscopical examination and described as Creataceous Limestone. Mr. C. N. Bromehead commented that the fluorine mineral is volcanic ash, which should have been found on this limestone; and is, in fact, dusted over the ridge of a hill, which overlooks the village and which forms the gathering ground of the local water supply. This ash is said to contain from 0·25 per cent. to 0·96 per cent. fluorine.

The Water. The water is derived from four deep wells. It is not treated in any way. Routine chemical analysis revealed no abnormality. The fluorine content was estimated by the Barr and Thorogood colorimetric method (Suckling, 1942) and found to be 7 parts per million. It is generally agreed that lesions occur where the concentration rises above 1 part per million, and Dean (1934) holds that such a figure would be accompanied by well marked lesions. Samples should be collected in containers of glass free from soluble fluorides.

Apart from changing the water supply as a preventative measure, it is possible to treat the water with calcium phosphate, manganese oxide, or aluminium phosphate.

Pathology. Fluorides are found in breast milk and can be recovered from the urine. Affected teeth and bones show an increase in their fluorine content. Enamel changes alone are to be found in childhood and are associated with delayed dentition. The enamel lesions appear to be due to the toxic effect of fluorine upon the ameloblasts of the enamel organ, causing their destruction and changes in their arrangement, together with subsequent imperfect calcium precipitation in the preprismatic fibres. At the same time the interstitial tissue is defective, making the teeth friable and causing bundles of prisms to be shed with the formation of pits. The brown stain is probably due to the deposition of food constituents between the prisms.

Symptoms. Apart from the unsightly appearance of the teeth, there are no symptoms in childhood. The early destruction of the teeth and crippling rheumatic symptoms arising out of bony changes, which occur later in adult life, however, make this condition one of some importance.

Local treatment is directed to improving the appearance of the teeth (where the stain is slight) with 12 per cent. HCl or filing the enamel surface. Usually, however, the teeth have ultimately to be extracted. Maintenance of the nutrition of the child is of particular importance.

Summary

The main features of a series of cases of dental fluorosis are described as they were presented among the children of a small village. The more important points which emerge are:

1. The appearance of ' brownin ' is the most striking and certain indication of the presence of the condition. It was this appearance which attracted the attention of Ainsworth (1933) in England.

2. ' Brownin ' closely resembles tobacco staining, but among children, where it develops slowly, the pigment is confined to the outer surface of the upper teeth.

3. Of the lesions noted (pitting, mottling, chalk patches and ' brownin ') only the latter can be produced by fluorosis alone. Differential diagnosis is given in the case of the other lesions and it is to be noted that the coexistence of acute infections and nutritional defects in infancy render the precise

estimation of the amount of fluorosis prevailing in a locality difficult.

4. The lesions occur on the permanent teeth only.

5. No evidence of osteo-arthritis was observed among the children.

6. The incidence of dental caries was low (2·7 per cent.).

7. Endemic goitre was present in the district.

8. Clinical findings were confirmed by finding fluorine present to the extent of 7 parts per million in the water.

Acknowledgment is made to Mr. C. N. Bromehead of the Geological Survey and Museum, London; to Dr. A. Stewart of the Royal Institute of Public Health and Hygiene, London; and to Dr. Margaret Murray of Bedford College, London, for information and help with the investigations.

References

Ainsworth, N. J. (1933). *Brit. dent. J.*, **55,** 233.
Churchill, H. V. (1931). *Ind. and Eng. Chem.*, **23,** 996.
Crighton-Brown (1892). *Lancet*, **2,** 6.
Dean, H. V. (1934). *J. Amer. dent. Ass.*, **21,** 1921.
Eager, J. M. (1901). U.S. Public Health Report, **16,** 2576.
Kemp, F. H., Murray, M. and Wilson, D. C. (1942). *Lancet*, **2,** 92.
McKay, F. S., Black, G. V. (1916). *Dental Cosmos*, **58,** 129.
Pillai, Rajogopalan, and De (1944). *R. Ind. med. Gaz.*, **79,** 248, 261.
Roholm, K. (1937). Fluorine Intoxication, London.
Sprawson, E. and Collier (1942). Dental Anatomy and Pathology Ed. 8. London.
Suckling, E. V. (1943). The Examination of Waters and Water Supplies, Ed. 5, London, 317.
Wilson .D. C. (1941). *Lancet* **1,** 211.

PYOCOLPOS IN INFANCY

BY

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Pyocolpos is rare at any age; in infancy it is extremely uncommon, and it is therefore desirable that every case should be reported, since the treatment is very simple when once the condition has been recognized.

Pyocolpos may be defined as ' a congenital atresia of the vaginal orifice, with retention of an excess of secondarily-infected cervical secretions '.

Case report. D. S., born June 26, 1945, was admitted to hospital at the age of 7½ hours. It was noticed, at birth, that ' something came down ' into the vulva when the baby cried; it was for this reason that the child was sent immediately to hospital. She had not passed urine or faeces.

ON EXAMINATION. The child appeared to be quite healthy; the only abnormality found was that at the vulva. There was no abdominal swelling. Local examination revealed a cystic mass, anterior to the fourchette; this was assumed to be protruding or prolapsing from the vagina. It obscured the urethra. The labia majora and minora were normal. The swelling became more prominent when the child cried. The house-surgeon observed that a probe could be passed up some distance anteriorly; this suggested the diagnosis of rectocoele. Digital examination of the rectum showed, however, that there was no prolapse of the anterior wall of the rectum. The most likely diagnosis, therefore, appeared to be that of cyst in the rectovaginal septum.

The infant soon passed urine and faeces normally, and was discharged to attend the Out-patient Department.

She was re-admitted on October 6, 1945, at the age of 3½ months, in poor condition, having passed no urine for twenty-four hours. Examination showed the same condition as before; but, in addition, there was a large tumour in the mid-line of the lower abdomen, almost reaching the level of the umbilicus. It was assumed that the tumour was the bladder, and the child was taken at once to the operating theatre and was examined under anaesthesia. The urethra was found with some difficulty, since it had been pulled upward. A silver catheter was passed. Concentrated urine flowed; but though the tumour became smaller it did not disappear, and a cystic mass remained, in the mid-line and arising from the pelvis. Fluctuation could not be elicited between this swelling and the vulval tumour.

Nothing more was done for the time being owing to the child's poor condition. Catheters were passed without difficulty three times in each twenty-four hours for several days.

The abdomen was opened on October 10, 1945, through a left lower para-median incision. The bladder presented; it was aspirated. The wall was thickened, loculated and trabeculated. Just behind the bladder, and attached below by peritoneum, was a firm, cystic swelling in the mid-line; this was surmounted by a small, undistended uterus, with normal adnexae.

Cross-fluctuation was found to be present between this and the vulval swelling. The latter was then aspirated; pus was withdrawn. An incision was, therefore, made into it, and a Malecot catheter was inserted. Much very foul-smelling pus was evacuated. The abdominal tumour, which was obviously the distended vagina, collapsed. The laparotomy wound was then closed.

The child recovered well from the operation.

The pus contained a large number of gram-positive cocci and B. proteus vulgaris. The cavity was, therefore, washed out twice a day with saline solution, and Penicillin was instilled. The discharge ceased on October 31, and the catheter was removed. The vaginal orifice was dilated under anaesthesia; the vagina was found to be abnormally long, but the cervix was normal.

The infant was discharged on November 4, 1945, and has since then attended the Out-patient Department twice. She is now well and is gaining weight, and the vaginal orifice appears to be normal.

Discussion. The condition, in this case, seems to have been one of true pyocolpos, for the uterus was not involved in any way. This was not so in the four uninfected cases reported by Mahoney and Chamberlain (1940), though they had an opportunity of examining two of their specimens histologically. They found that the condition was due to atresia of the vaginal orifice, comparable with imperforate anus, and not to imperforate hymen. This would be more in keeping with embryological evidence.

It is interesting, in the present case, to postulate the mode of infection of the closed cavity. The infection was, in all probability, blood- or lymph-borne from the lower bowel.

Very few cases of this type have been recorded. Commandeur (1904) quoted ten cases by various authors. Cranwell (1905), Bjerrum (1915), Spence (1916), Bonnet (1930), and Mahoney and Chamberlain (1940) have reported cases since then; some of them were infected, though the majority were not.

A case similar to that now recorded has

recently been treated at King's College Hospital.

A cystogram, as suggested by Mahoney and Chamberlain, is a useful aid to diagnosis; it shows the gross forward displacement of the bladder. More important, however, is the recognition of the clinical entity; and then follows the treatment, which is both simple and effective.

Summary. A case of pyocolpos in infancy is recorded. The symptoms and signs of the condition, and its treatment, are given. Stress is laid upon the importance of recognition of the clinical condition, and upon the simplicity and adequacy of the treatment.

I should like to thank Mr. T. Twistington Higgins and Mr. Alan Small for their permission to publish this case.

References

Bjerrum (1915). *Ugesk. f. Laeger. Kbenh.*, **77**, 407.
Bonnet, A. (1930). *Thesis*, Paris.
Commandeur, M. (1904). *Bull. de la Soc. d'Obstet de Paris*, **7**, 54.
Cranwell, D. J. (1905). *Rev. Gynec. et de' Chir. abd.*, **9**, 635.
King's College Hospital (1946). *Personal communication.*
Mahoney, P. I., and Chamberlain, J. W. (1940). *J Pediat.*, **17**, 772.
Spencer, H. R. (1916). *Lancet*, **1**, 823.

REVIEWS

Napt Handbook of Tuberculosis Activities. Edited by HARLEY WILLIAMS, M.D. 12th Edition, revised and enlarged, with Commonwealth and Empire Supplement. 1946. London, National Association for the Prevention of Tuberculosis. Pp. 276. (Price 7*s.* 6*d.* net.)

This is described as 'The only complete Directory of Dispensaries, Clinics, Sanatoria, etc.,' and it may well be so. It deals with Local Authority tuberculosis schemes, mass radiography units, centres for thoracic surgery, sanatoria and hospitals for the treatment of tuberculosis in Great Britain and the Commonwealth and Empire, the activities of the NAPT, organizations interested in tuberculosis, the veterinary service in Great Britain, District Rehabilitation Offices, and journals on tuberculosis. It is essentially a work of reference, giving, for instance, the address, number of beds, staff, etc., of institutions admitting cases of tuberculosis in each area. It does not aim at giving any critical evaluation of the services available.

Aerosols in Theory and Practice. By ARCHIBALD C. LOCK, M.I.E.E. Phantosol Products Limited, London. Cloth, pp. 40. (Price 5*s.*)

Although to some extent concerned with those aspects of aerosol distribution and the apparatus which particularly concerns the publishers, this little work differs from the majority of productions of its kind by giving the reader a really clear, unbiassed summary of the subject. Put very briefly an aerosol is a mist, so finely particulate that it does not wet the surfaces it meets, remains suspended in the air for long periods and penetrates into remote corners. According to its chemical composition an aerosol may be used for various purposes. Thus pyrethrum, lethane and now D.D.T., dispersed either by the 'Freon Bomb' or by the author's own electrically driven apparatus, are known to be highly effective in killing insects such as aeroplane-borne mosquitoes or those found in stores of tobacco, cocoa, flour and other commodities. It has been shown by Trillat, Mudd, Pulvertaft, Twort and numerous other observers that aerosols containing the glycols, resorcinal or the hypochlorites and dispersed into the atmosphere of rooms will rapidly reduce the number of suspended viable bacteria which can be recovered from the atmosphere. Finally, as noted in the last number of this Journal in connection with aerosol penicillin dispersed in oxygen tents, a water-soluble drug inhaled in aerosol form can be readily absorbed via the lungs. As an insecticidal method the aerosol technique has already proved itself. The menace of cross infection through dust is sufficiently serious in hospital, particularly paediatric, practice to make the bactericidal application deserving of full systematic trial. Pure laboratory experiment has already given highly favourable results, and one awaits with interest the large-scale 'field trials' which are most certainly worth making. Absorption of drugs by inhalation which, for their administration, have so far required repeated injections opens up obvious and very numerous possibilities. The author is certainly dealing with a method which probably has applications considerably wider than is at present generally appreciated in the medical world, and one can therefore recommend this summary as providing a highly useful introduction to a subject of the future.

The Newborn Infant. *A manual of obstetrical pediatrics.* By EMERSON L. STONE, M.D. Associate Clinical Professor of Obstetrics and Gynecology, School of Medicine, Yale University; Attending Obstetrician and Gynecologist to the New Haven Hospital. Third Edition, thoroughly revised. 1945. London, Henry Kimpton. Pp. 314. (Price 16*s.* 6*d.* net.)

The author defines the aims of this work as being the correlation and orderly arrangement of a mass of data otherwise scattered through the literature, the emphasizing of the obstetrician's viewpoint and responsibility, and the extension of his interest in this branch of his subject. It may be said at once that in the realization of these aims Dr. Stone has been singularly successful. The first chapter deals with the immedate care of the newborn, and includes a discussion on the treatment of asphyxia. This is followed by a useful section on the physiology of the newborn, after which the book follows the orthodox arrangement, viz. breast and artificial feeding, diseases of the various systems, and a final section on the premature infant. It is obvious that the author has read widely and critically; the numerous references are well chosen, and there is little recent work of established value which is not referred to. Obviously certain aspects of the subject, e.g. infant feeding, will be dealt with more fully and adequately in other works, but within the compass of one volume the author has certainly provided a most valuable handbook for those dealing with the newborn infant, either as obstetricians or paediatricians.